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KEY TO ABBREVIATIONS

c — correspondence
 cr — case record
 e — editorial
 mdph — Massachusetts Department of Public Health

MMS — Massachusetts Medical Society
 mp — medical progress
 misc — miscellany

n — notice
 o — obituary
 * — original article

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CASE RECORDS
OF THE MASSACHUSETTS GENERAL HOSPITAL
WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B MALLORY, M D , *Editor (on leave of absence)*
BENJAMIN CASTLEMAN, M D., *Acting Editor*
EDITH E PARRIS, *Assistant Editor*

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1945

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SURGICAL MANAGEMENT OF CARCINOMA OF THE MIDTHORACIC ESOPHAGUS*

Preliminary Report

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BOSTON

IN OCTOBER, 1942, in an address given before the American Academy of Ophthalmology and Otolaryngology, I¹ made the following statement:

Adequate removal of a carcinoma located in the middle half of the esophagus precludes the possibility of performing an anastomosis within the chest for the restoration of continuity. In all these cases it is necessary to establish a cervical esophagostomy and a gastrostomy or enterostomy for feeding.

Two years later, as a result of increased experience with the transthoracic resection of carcinoma of the cardia and lower end of the esophagus, the field of resection followed by an anastomosis has been enlarged and a satisfactory technic for the removal of malignant lesions higher in the esophagus has been developed. The Torek procedure can therefore be discarded except in those relatively rare cases in which the lesion extends well above the aortic arch.

The Torek operation, originally described in 1913,² has had a limited use. There are two serious objections to this procedure. In the first place, if it is carried out according to Torek's original technic which involves cutting across the lower esophagus and not entering the abdominal cavity, two important groups of lymph nodes to which these tumors frequently metastasize are not removed, these are the subdiaphragmatic periesophageal nodes and the group found in relation to the left gastric vessels.

TABLE 1 Abdominal-Node Metastases in Carcinoma of the Esophagus (72 Autopsied Cases)

LOCATION OF TUMOR	NO. OF CASES	ABDOMINAL NODES	
		POSITIVE	NEGATIVE
Upper third (neck and upper chest)	24	1	23
Middle third	32	11	21
Lower third	16	8	8

(Fig. 1) As a result, the operation is hardly worth while because these nodes are so frequently involved (Table 1). If one takes into account the

additional fact that the resectability of carcinoma in the midesophagus is perhaps the lowest of any region in the body, being found in only 14 per cent of all patients seen,¹ the possibility of obtaining a cure or a reasonably long remission of symptoms is

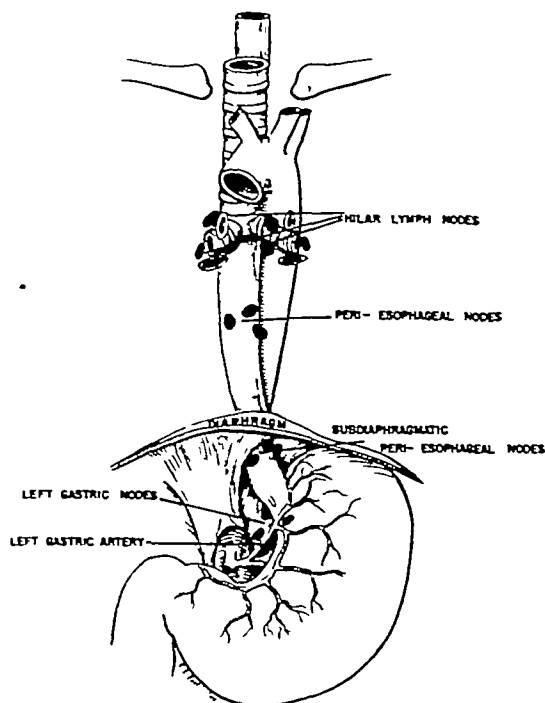


FIGURE 1 The Most Frequent Sites of Lymph-Node Invasion in Cases of Carcinoma of the Esophagus (reproduced from Sweet,³ by permission of the publisher)

discouragingly remote. The principal hope in such cases is for worth-while palliation.

The second major objection to the Torek operation is that as a palliative procedure it is most unsatisfactory. The continuous discharge of saliva and mucus through the cervical esophagostomy stoma and the trouble attending the care and the use of the gastrostomy for feeding make the patients who have been subjected to this operation miserable

*From the Surgical Service of the Massachusetts General Hospital and the Surgical Service of the Palmer Memorial Hospital. Presented at the annual meeting of the New England Surgical Society, Boston, September 20, 1944.

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and unhappy. If the use of a rubber-tube connection is attempted, there may be leakage around the tube, difficulty in keeping it adjusted and inability of the patient to eat anything but liquids because of the mechanical inadequacy of the system. Even if, after much effort on the part of the surgeon and with hope and fortitude on the part of the patient, an external plastic esophagus is constructed, the length of time required makes the procedure impractical. In some cases, by the time the patient is able to take a soft diet and swallow the food through such a tube, he is already suffering the effects of recurrent or metastatic disease.

TOREK PROCEDURE

Since January, 1940, Torek operations have been performed on 14 patients at the Massachusetts General and Palmer Memorial hospitals. There were 2 postoperative deaths and 12 survivals. In 4

esophagus (Fig 2). These results have been discouraging.

RESECTION FOLLOWED BY HIGH ESOPHAGOGASTRIC ANASTOMOSIS

New hope has arisen from the application of knowledge gained from a large experience with resection of the cardia and lower esophagus by the transthoracic route. As a result, it is now possible to perform a much more radical esophagectomy in such cases, including the removal of the lymph nodes below the diaphragm, and to restore immediately the continuity of the gastrointestinal tract by an esophagogastric anastomosis performed high in the chest.

Technic of Operation

With the patient lying on his right side, the eighth rib on the left is resected and the seventh, sixth and,

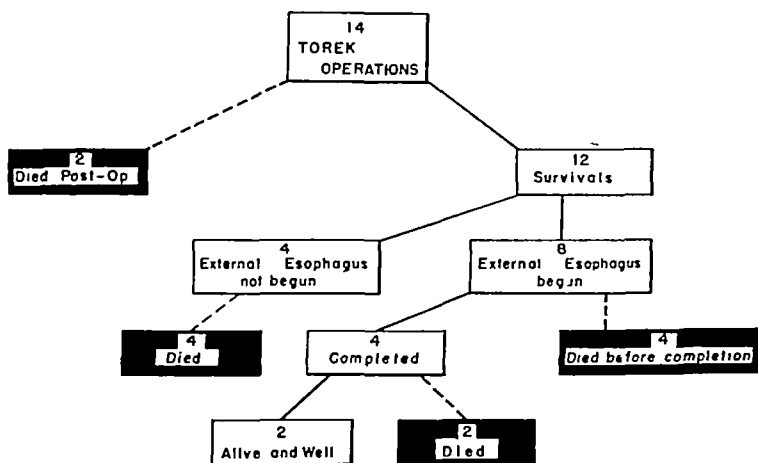


FIGURE 2 Experience with the Torek Operation at the Massachusetts General Hospital

cases, an external esophagus was completed, a connecting tube constructed from the skin of the chest wall with additional grafts from the thigh being utilized. This tube was used in 2 cases to connect the proximal esophagostomy opening above with a Beck-Jianu gastrostomy below. In 1 case, the lower esophageal end, pulled up to the anterior abdominal wall, was used as the lower stoma, and in 1 the fundus of the stomach and the stump of the esophagus were used after being pulled up under the skin of the chest wall.¹ Two patients died of metastases soon after the completion of the external esophagus. Two were alive and well 4 and 2 years, respectively, after operation. Of the remaining 8 patients, 4 died during the period of construction of the external esophagus—1 of pneumonia that did not respond to sulfonamide chemotherapy, and 3 of metastases or local recurrences. The remaining 4 patients have died of their disease without any attempt's being made to construct an external

if necessary, fifth ribs are divided posteriorly. This incision provides an adequate exposure to the region of the growth, and at the same time gives room enough below for incision of the diaphragm and mobilization of the stomach so that it can be brought up for an anastomosis high in the thorax.

Because of their location so close to several vital structures, such as the aorta, the inferior pulmonary vein, the left main bronchus and the left pulmonary artery, many of the tumors in this location are inoperable owing to direct invasion of these structures. It is therefore best to explore first the region of the growth. If one is careful, the possibility of completely mobilizing the tumor-bearing portion of the esophagus can usually be determined before division of any of the segmental esophageal arteries, which arise from the aorta. Once the resectability of the growth has been established, these vessels can be cut and the entire mass freed. In carrying out the mobilization of the growth, an opening into the

right pleural cavity is often made. At times it is necessary to remove a portion of the mediastinal pleura of the right side because of its adherence to the growth. The anesthetist's positive pressure prevents any serious degree of collapse of the right lung in such cases, and no attempt to close the opening need be made, because once the chest-wall incision is made airtight by its closure, there is no further danger of collapse of either lung unless lung tissue has been injured so as to permit escape of air from the alveoli.

After the midesophagus has been completely mobilized, the diaphragm is incised from the costal insertion through the hiatus. The upper portion of the stomach is then mobilized by dividing the post-

throughout its wall, especially at its upper portion. Furthermore, and for the same reason, the incision across the stomach must be at or just distal to the cardia, thus minimizing the danger of interrupting any anastomotic vascular channels within the stomach wall. Nevertheless, even in these cases one can with care remove the major portion of the lymph nodes around the cardia and from the region of the left gastric vessels.

Once the mobilization is complete, the stomach is cut across at or just below the cardia; its cut end is inverted, and a rubber glove is tied over the proximal end to avoid soiling the field of operation. If there is 5 cm or more of normal esophagus between the aortic arch and the superior margin of the

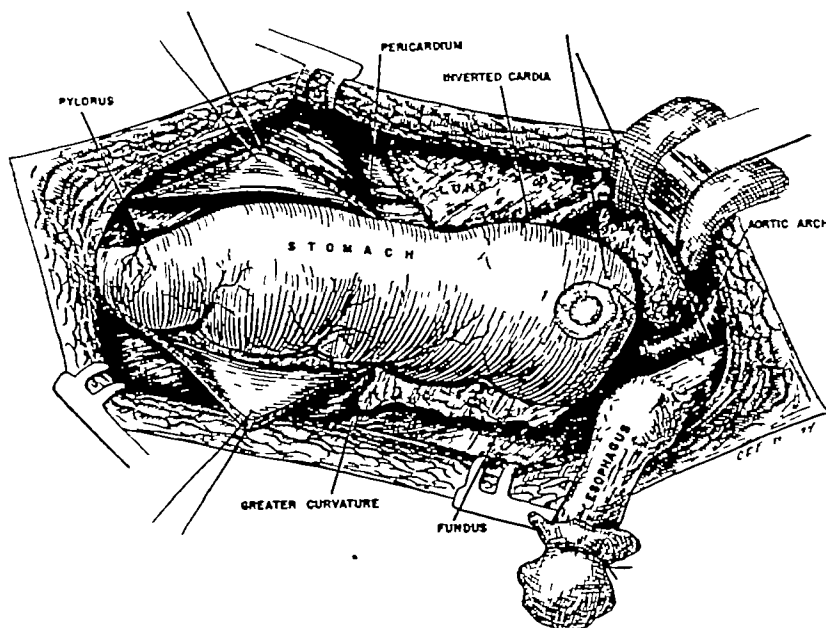


FIGURE 3 High-Esophago-gastric Anastomosis for Carcinoma of the Midthoracic Esophagus (reproduced from Sweet,² by permission of the publisher)

The esophagus has been completely mobilized and pulled out from behind the aortic arch. The stomach, after complete mobilization preserving the right gastric and right gastroepiploic vessels, is shown pulled high into the chest so as to make possible an anastomosis at or just above the level of the aortic arch.

cardial attachments, the vasa brevia, the gastrolienal and gastrohepatic ligaments and the left portion of the gastrocolic ligament. In all cases the ascending branches of the left gastric vessels must be severed to make it possible to swing the fundus far enough into the thorax to permit a high anastomosis.

In some cases in which the growth is unusually high, so that the esophagus must be divided close to or even above the aortic arch, it is necessary to divide the left gastric artery close at its origin and to cut the left gastroepiploic artery. I have proved by actual performance that this can be done with a successful outcome. The stomach must, however, be handled with great care to avoid trauma to any of the vessels that enter into the anastomosis.

growth, it is usually possible to perform an esophago-gastric anastomosis just below the aortic arch. If, on the other hand, the growth extends nearer to the arch, an anastomosis becomes impossible unless the esophagus is pulled up from behind and the anastomosis is performed in front of the aortic arch or at the level of its superior margin. In January of this year Garlock³ reported such a case. The usual three-layer, silk-technic anastomosis is performed, with excision of a circular piece of the wall of the fundus of the stomach. The technical details of this operation have been described elsewhere.^{4, 5}

This operation in cases of carcinoma of the mid-thoracic esophagus approaches more closely than anything previously available the ideal procedure for the radical removal of the tumor, including the

majority of the regional lymph nodes, for more satisfactory palliation in incurable cases, and for the obtaining of a better functional result

Experience in Carcinoma of the Midthoracic Esophagus

Since we have learned how to free the stomach sufficiently to bring the fundus to the level of the aortic arch or even above it, resections followed by high anastomosis have been carried out in 9 patients at the Massachusetts General and Palmer Memorial hospitals. In 5 of these cases, the upper limit of the growth was at a level that made it possible to perform an esophagogastric anastomosis just below the aortic arch. One of these patients died suddenly of what was apparently coronary thrombosis (permission for autopsy was refused)

this new operation, the last case mentioned is reported in detail

C K (M G H 444,523), a 63-year-old woman, was seen for the first time on May 17, 1944. For 4 months she had been having difficulty in swallowing, the trouble beginning with solids but gradually increasing until she could swallow nothing but liquids, even then she had to drink very slowly. She had lost a great deal of weight and strength.

Physical examination was essentially negative except for emaciation. The weight was 94 pounds. The heart sounds were regular and of good quality, with no murmurs. The blood pressure was 120/80. The diaphragm was low and moved only 1 cm. or less. Chest expansion was poor.

The patient was admitted to the Baker Memorial on May 19. On admission the white-cell count was 5400, the red-cell count 3,690,000, and the hemoglobin (photoelectric method) 11.0 gm. The nonprotein nitrogen was 32.5 mg. per 100 cc., the serum protein 6.0 gm., and the blood chloride 93 milliequiv. per liter. A blood Hinton test gave a negative reaction. X-ray examination revealed an ulcerating lesion in the middle

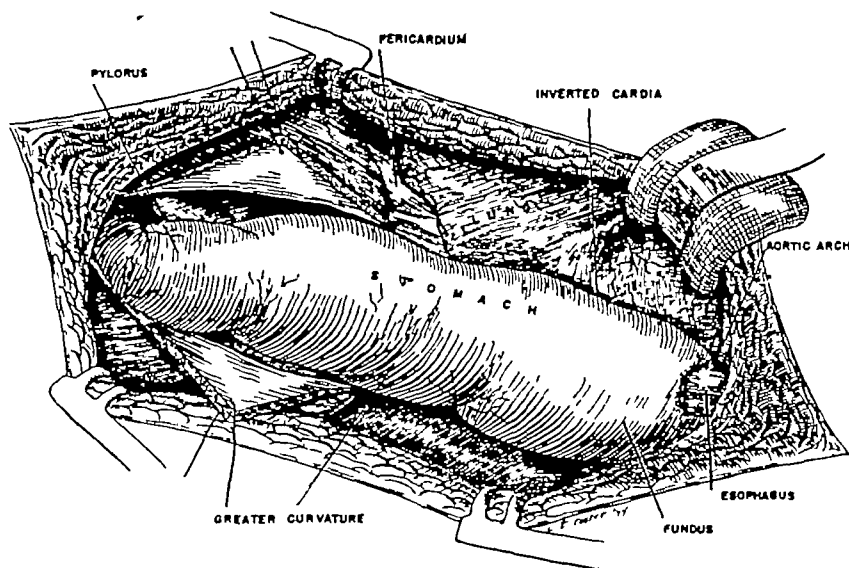


FIGURE 4 The Completion of a High Ante-aortic Esophagogastric Anastomosis (reproduced from Sweet,³ by permission of the publisher)

One is still in the hospital. The remaining 3 were doing well a few months to somewhat over a year from the date of operation.

In the remaining 4 cases, it was impossible to perform an anastomosis below the aortic arch, so that the upper end of the esophagus had to be mobilized and pulled up in front of the arch (Figs 3 and 4). The level of the completed anastomosis was at the superior margin of the aortic arch. Two of these patients died in the hospital, one because of sepsis resulting from tearing into an extremely adherent and actually inoperable growth during the operation, and the other because of coronary thrombosis (proved by autopsy). Of the 2 patients who survived the operation, one died subsequently of metastatic carcinoma, and the other recovered completely and resumed work.

As an illustration of what can be accomplished in cases of carcinoma of the midthoracic esophagus by

third of the esophagus, the appearance being consistent with a malignant tumor (Fig 5).

Esophagoscopy, performed by Dr. Edward B. Benedict, showed an annular, proliferating, nodular mass arising mostly from the left wall of the midesophagus, apparently not fixed and only partially obstructing the lumen. Its appearance was characteristic of carcinoma. Biopsy specimens were reported by the pathologist as epidermoid carcinoma, Grade III.

Intravenous infusions of glucose in saline solution and of amino acids (Amigen), as well as transfusions of blood, were given. The patient was able to take a high-calorie liquid diet. Parenteral vitamins were administered by the intravenous route. During the 48 hours immediately preceding operation sulfadiazine was given.

At operation, performed on May 27, an oblique incision was made across the left side of the chest and the 8th rib was resected. To obtain adequate exposure the 7th, 6th and 5th ribs were divided posteriorly. The growth was found lying in the esophagus and extending from just below the level of the aortic arch to a point opposite the inferior pulmonary vein. It was densely adherent to the areolar tissues over the aorta, and at one point it was necessary to cut so close to the aorta that one of the esophageal arteries was cut flush with its wall. The bleeding from this vessel had to be controlled by means of two sutures of arterial silk. After much painstaking dis-

section the growth was freed from the aorta. It was dissected from the hilus of the lung with greater ease, although there was a certain amount of adhesion to the structures just behind the left main bronchus. After the midportion of the esophagus had been freed all the way above the aortic arch, it was decided that a resection could be carried out.

After the phrenic nerve had been pinched, the diaphragm was incised. The spleen was freed from the stomach by cut-

ting the vasa brevia and the left gastroepiploic vessels, the former of which were extremely short. There were two or three enlarged, hard lymph nodes in the region of the left gastric vessels making it necessary to divide these vessels close to their origin to remove the nodes. Thus the stomach was entirely severed from its blood supply except for the right gastric and the right gastroepiploic vessels. A clamp was put across just distal to the cardia in such a way as to include all the involved lymph nodes in the excised portion. A second clamp was put on and the stomach was cut between them. A square of rubber dam was tied over the proximal cut edge. The distal edge was sutured, a fenestrated clamp being used. A second layer of catgut was used to invert the sutured edge, and a final layer of interrupted silk sutures was applied.

The stomach having been freed, it was possible to pull it up to a point just above the aortic arch. The esophagus was pulled up from behind the aortic arch and around in front of it. A circular incision was made close to the apex of the fundus of the stomach, and a three-layer, interrupted-silk, end-to-side anastomosis was carried out that after completion lay opposite the superior margin of the aortic arch. The stomach was fixed in the chest by interrupted silk sutures between it and the pleura lateral to the aorta. No attempt was made to close the opening that had been made in the right pleural cavity. The liver was palpated, nothing abnormal being found. The diaphragm was loosely attached to the stomach and the remaining portion of the diaphragm was closed. A catheter was led out through the lower part of the chest, its tip being placed behind the stomach in the right pleural cavity. A hole was made in the side of the catheter so as to drain the left pleural cavity and after the lung had been expanded the chest was closed, using silver wire in the 7th rib to help maintain rigidity. The remainder of the wound was closed with silk.

Pathological examination showed the specimen to consist of a previously opened segment of esophagus 11 cm long, with a 2 cm cuff of normal-appearing gastric mucosa. Five centimeters above the cardioesophageal junction was a firm ulcer 3 cm in diameter that completely surrounded the esophageal wall, its base was reddish-gray and granular. The mucosa-covered ulcer margins were raised and indurated. The cut surface was grayish white and granular, and the lesion extended into the surrounding fascia. The upper border of the ulcer was 2 cm from the esophageal incision line. In the portion of esophagus just distal to the main lesion there were several small, indurated, yellowish brown, submucosal nodules measuring 3 to 5 mm. There were many shaggy, yellowish gray lymph nodes measuring 1 to 2 cm scattered over the posterior aspect of the tissue, some of them hard and others cystic and necrotic on section. Eight of these were removed from various areas for section. Microscopical examination showed the tumor to be epidermoid carcinoma,



FIGURE 5 Roentgerogram (Patient C K)

The thoracic esophagus shows a filling defect caused by a carcinoma in the middle of the thoracic esophagus.



FIGURE 6 Resected Specimen (Patient C K) (reproduced from Sweet,³ by permission of the publisher)

This includes the esophagus, which contains the tumor, the cardia and a portion of the fundus of the stomach. Three groups of enlarged lymph nodes can be seen attached to the gastric end of the specimen.

Grade III, with metastases to the regional lymph nodes (Fig. 6).

The patient's immediate recovery from operation was uneventful. During the first 4 days she experienced enough respiratory embarrassment to require the continuous use of an oxygen tent, but after that time there was no difficulty and the convalescence was free from complications.

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The patient returned to work, and at the last examination, several months after operation, was well and had gained 12 pounds in weight.

Figures 7 and 8 are reproductions of postoperative roentgenologic films showing barium in the esophagus and stomach.



FIGURE 7 Roentgenogram (Patient C K)

This anteroposterior view, taken four months postoperatively, shows that the level of the esophagogastric anastomosis is considerably above that of the aortic arch and illustrates the fact that the major portion of the stomach lies within the chest.

The high level of the anastomosis opposite the manubrium of the sternum is shown especially in the lateral view (Fig. 8). Almost the entire stomach lies in the chest.

SUMMARY

The classic Torek operation is subject to the objections that it does not make provision for radical removal of the regional lymph nodes, which are so frequently invaded by disease, thus diminishing the possibility of obtaining a cure, and that it fails to provide satisfactory palliation because of the discomfort and unhappiness of the patient that result from the presence of a cervical esophagostomy and the necessity of being fed by gastrostomy. The construction of an external esophagus to connect the two stomas is a long and tedious process, usually performed in several stages, and can rarely be completed except in the most favorable cases.

Experience with 14 cases in which the Torek operation was performed is set forth.

Resection of the entire esophagus below the level of the aortic arch, followed by a high esophago-gastric anastomosis either just below or just above the level of the aortic arch, offers a more nearly ideal solution of the problem of the surgical removal of carcinoma of the esophagus, since it facilitates radical removal of the tumor, including the majority of the regional lymph nodes, and provides a more satisfactory degree of palliation in incurable cases and a better functional result.

A summary of the results of this operation in 9 cases is given, and a case is reported in detail as an illustration of what can be accomplished with this relatively new procedure.

During the interval of time that has elapsed since this paper was read before the New England Surgical Society, 11 additional patients have been subjected to radical operation for carcinoma of the middle half of the thoracic portion of the



FIGURE 8 Roentgenogram (Patient C K)

The lateral view, also taken four months postoperatively, shows that the esophagogastric anastomosis is opposite the manubrium of the sternum.

esophagus. In 3 of these the anastomosis was performed just below the aortic arch, and in 8 of them the growth extended so high that it was necessary to perform the anastomosis above

the aortic arch. Recovery was uneventful in 8 cases, complications occurred in 3, and these patients died. The causes of death in these cases were chylothous hydrothorax, empyema and cardiac failure, respectively. All deaths occurred in patients with high growths, which required anastomosis above the aortic arch.

The inclusion of these 11 additional cases makes a total series of 20 cases of carcinoma of the midthoracic esophagus with resection followed by high esophagogastric anastomosis. In 8 of these an anastomosis just below the aortic arch was performed, whereas in 12 it was necessary to relocate the esophagus and perform the anastomosis above the aortic arch.

In the entire series there were 6 deaths, a mortality of 30 per cent. Thirteen patients recovered and left the hospital in good condition, and 1 is still in the hospital.

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DISCUSSION

DR. FRED B. LUND, Boston. This is one of the most brilliant presentations I have ever heard. Some years ago I had an opportunity to see at the Nose and Throat Department of the City Hospital all the cases of cancer of the esophagus that came there and of the 35 cases, 3 appeared to be operable. I operated on one patient through the chest, when I found that the growth had invaded the aorta, I did nothing more and the patient died. In the second case, I did a Torek operation, incising the pleura and sewing it up, the patient died. In the last case, I did a Lilienthal operation through the back and this patient also died. All these cases had presented poor prospects, but even so I was rather discouraged. Nevertheless I should have continued to operate if more operable cases had presented themselves.

DR. HARLAN F. NEWTON, Boston. It is well known to every one of us that the esophagus has been the "soft spot of the underbelly" of surgery. We have all heard and read of the splendid results in the surgical treatment of carcinoma of the upper third of the esophagus by excision that have in the past few years come from Canadian surgeons. Also, the lower third of the esophagus, attacked by cancer, has frequently been treated by excision with success. Dr. Sweet's paper deals with the surgical excision of carcinoma of the midesophagus, a tumor that has been considered up to this time as hopelessly inoperable. This makes his contribution outstanding and a pioneer piece of work.

The esophagus does not lend itself well to healing following operative trauma because of poor tissue resistance, friability, leaks following anastomoses, mediastinitis and other complications. Also of tremendous importance are the high degree of malignancy and the high incidence of early metastasis of practically every esophageal carcinoma.

Dr. Sweet is truly to be complimented both on this extraordinary series of cases so beautifully handled and for his modesty, for I know of no other such series of cases comprising

surgical excision of carcinoma of the midesophagus. We operated on a patient at the Peter Bent Brigham Hospital who has now gone about fourteen months without recurrence after complete resection of the carcinoma, this tumor originally appeared to be inoperable, but it was really at the junction of the lower and middle thirds of the thoracic esophagus.

Technically, excision of the midthoracic esophagus with mobilization of the stomach and anastomosis of the upper end of the esophagus to the stomach in front of the arch of the aorta is a brilliantly conceived, difficult achievement. It should stimulate all of us, particularly those interested in thoracic surgery.

I do not believe that we should even ponder on Dr. Sweet's results, and should certainly not criticize the mortality in his series. He is dealing with a lesion certain to kill and certain to kill rapidly. If he has extended any of these patients' lives and has increased their comfort, as is obvious from his results, surgery has been truly successful. In dealing with carcinoma of the esophagus in comparison to benign strictures there can be no choice between early one-stage esophageal anastomosis and multiple-stage surgery.

I think that Dr. Sweet considers this as only a preliminary report, in many ways a report of progress, but the fact that we have among us a man with courage enough to tackle this problem in a large series — and 9 is a large series — deserves commendation.

DR. DAVID CHEEVER, Boston. I wish first merely to pronounce the word "magnificent." During Dr. Sweet's discussion he uttered the words, "if you remember your anatomy." Dr. Sweet does remember his anatomy. I do not believe that he had to bone up on his anatomy before performing these operations.

Harvard Medical School students in the course of their instruction in anatomy have had called to their attention over many years the tremendous importance of the blood supply of the stomach and intestines. The points have been made that it is impossible to impair in the least degree the blood supply of the intestines and that, because there are so few anastomoses, one cannot resect freely, whereas in the stomach at least three fourths of the blood supply can be tied off the remaining fourth being sufficient to carry on the nutrition of the tissues, thus permitting extensive resections. Of course, it is this fact that, among so many others, Dr. Sweet has taken advantage of and that has made these magnificent results possible.

DR. RICHARD H. SWEET (closing). Both Dr. Newton and Dr. Fred Lund referred to operability, or at least implied that this was in their minds. Dr. Newton spoke about 9 cases being a large series, as a matter of fact, it is, because before we started doing this anastomotic work, I studied the operability of about 70 consecutive cases of carcinoma of the midesophagus that I had seen, and learned that only 14 per cent of the patients were finally subjected to a radical resection. Of course, the reasons for this are obvious. The principal one is the anatomic relation of the esophagus, these tumors lying opposite the pulmonary veins and arteries and the left main bronchus. Many actually invade these structures or the aorta.

With regard to entering the right pleural cavity, in case some of you wish to take up this type of surgery, the opposite pleura is frequently and of necessity opened, because, as you know, the pleura is reflected from both sides of the esophagus, but one need not pay any attention to this. One can open the right pleural cavity with safety, and nowadays I never bother to close it again, because the anesthetist has the situation under control.

I should like also to reiterate what Dr. Newton said. This is a preliminary report, and the whole subject is in a phase of development.

THE ANTITHROMBOTIC ACTION OF GELATIN*

Preliminary Report

HENRY HAIMOVICI, M D,† AND JACOB FINE, M D ‡

BOSTON

PROPERLY prepared gelatin is now regarded as a satisfactory blood substitute within certain limits for the treatment of traumatic shock.^{1 2} Intravenously administered gelatin, however, has been observed to produce an increased bleeding and clotting time in the experimental animal in deep shock.¹⁻³ This is also true of albumin and plasma.³ It occurred to us that if this were also a property of such fluids in the relatively normal state of the organism, they might prove useful in the prophylaxis or therapy of deep venous thrombosis, in place of heparin or dicoumarin, which have serious limitations. Of these fluids the most readily available is gelatin. This report deals with a preliminary experimental inquiry into the capacity of gelatin to prevent thrombosis in veins subjected to injury.

METHOD

The simplest method of producing thrombosis in a vein is by the use of a noxious chemical agent.^{4 5} Acceptable conditions for a study of the production of venous thrombosis by a chemical agent require that a given length of vein that has no branches be exposed to a given concentration of a given caustic agent for a given length of time. A sterile surgical technic is essential for this purpose.

Mongrel dogs weighing 8 to 10 kilograms were given morphine sulfate (10 to 20 mg per kilogram) or occasionally a 60 per cent Nembutal solution intravenously. Under novocain anesthesia the femoral or jugular veins or both were exposed aseptically. After 2.5 cm of each vein was carefully liberated from its sheath, two loops of thread were passed around it and the blood was gently milked from this segment. The vessel was then lifted by the threads, and into this temporarily isolated segment a quinine-urethane solution§ was injected through a 25-gauge needle and retained under slight tension within the lumen for periods varying from thirty seconds to five minutes. In most of the experiments a two-minute exposure was used. The fluid was then withdrawn into the syringe and the circulation re-established. At the completion of this procedure the wound was closed in two layers. Histologic examination of veins prepared as described, except for the actual injection of the quinine-

urethane solution, showed no injury to the intima or resulting thrombosis.

Intravenous pigskin gelatin solutions¶ were used exclusively. The various samples were fairly homogeneous in their simpler physical properties and chemical composition, with the following representative characteristics: dry weight, 7.17 per cent, ash, 0.95 per cent, sodium chloride, 0.85 per cent, reaction, pH 7.42, bloom, 41.0 gm, and viscosity, 3.4 at 37.5°C. Most of the solutions were autoclaved at 15-pounds pressure for forty-five minutes, and some for a longer period.

In the course of experimentation, twelve different preparations of gelatin were used. Eight of these exhibited definite antithrombotic action, whereas the other four, prepared somewhat differently, showed little ability to prevent intravascular clotting following injury. In the experiments reported below, only preparations known to be active were employed.

RESULTS

Control Experiments

In 13 dogs the intima of twenty-six veins was exposed to the quinine-urethane solution for thirty seconds. These veins were examined eighteen hours to six days after the operation. Ten veins (38 per cent) exhibited complete thrombotic occlusion, five (19 per cent) contained small nonoccluding thrombi, and eleven (42 per cent) were completely patent (Table 1). Failure to induce thrombosis uniformly in these experiments seemed to be due to the short exposure of the veins to the chemical injury. Accordingly, in subsequent experiments (thirty-one veins in 11 dogs) the exposure was increased to one to five minutes, in most of the experiments the time being two minutes. When the vessels were examined fifteen to forty-eight hours afterward, thrombosis was found in 84 per cent of the injured veins.

Macroscopic examination of the occluded veins showed at the site of injury a thrombus that, as a rule, did not propagate beyond the next proximal and distal branches. In only 2 cases was there found an extensive secondary clot, which in each extended from the jugular vein through the superior vena cava, right auricle and inferior vena cava and stopping at the hepatic veins.

Gelatin Experiments

In the experiments with gelatin the points under consideration were the volume and concentration

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†The expenses of this investigation were provided from a grant to Harvard University from the Edible Gelatin Manufacturers Society of America.

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¶Ampules of quinine urethane solution were kindly supplied by Abbott Laboratories, North Chicago, Illinois.

‡The gelatin solutions were kindly supplied by the Edible Gelatin Manufacturers Society of America.

of the gelatin solution necessary to prevent intra-vascular clotting (gelatin does not prevent clotting in vitro), the comparative value of gelatin injected before and after injury to the intima, and the period

the remaining five contained small, nonoccluding thrombi (Table 2)

In the second series, thirty-three veins in 12 dogs were used Fifty-two per cent of the vessels

TABLE 1 Control Experiments

EXPOSURE TO QUININE URETHANE	No OF DOGS	No OF VEINS	VEIN PATENT	PARTIAL OCCLUSION OF VEIN	COMPLETE OCCLUSION OF VEIN	PARTIAL AND COMPLETE OCCLUSION OF VEIN
30 seconds	13	26	42	19	38	58
1-5 minutes	11	31	16	3	81	84
1 min		8	0	0	100	
2 min		21	23	5	71	
3 and 5 min		2	0	0	100	

during which the prophylactic action of gelatin remained effective

Several series of experiments were carried out with these objectives in mind In the first series, 50 cc of gelatin per kilogram of body weight was injected intravenously one to two hours before injury to the veins In the second series, the same

were patent, 16 per cent were partially occluded, and 31 per cent were completely occluded Further analysis of this series showed that of the twenty veins subjected to the action of gelatin between four and a half and seven hours before injury, only one showed complete occlusion, whereas of thirteen veins subjected to the action of gelatin between

TABLE 2 Gelatin Experiments

TYPE OF INJECTION	EXPOSURE TO QUININE-URETHANE	No OF VEINS	VEIN PATENT	PARTIAL OCCLUSION OF VEIN	COMPLETE OCCLUSION OF VEIN	PARTIAL AND COMPLETE OCCLUSION OF VEIN
			%	%	%	%
Intravenous gelatin 50 cc./kg 1 to 2 hr before injury to vein (17 dogs)	1 min	11	100	0	0	
	1½ min	8	88	12	0	
	2 min	5	100	0	0	
	3 and 4 min	6	67	33	0	
	5 min	5	60	40	0	
		35	86	14	0	14
Intravenous gelatin 50 cc./kg. 4½ to 9 hr before injury to vein (12 dogs)	1 min	2	50	50	0	
	2 min	31	52	16	31	
		33	52	18	30	48
Intravenous gelatin 25 cc./kg 1 to 3 hr before injury to vein (14 dogs)	1 and 1½ min	7	0	71	29	
	2 min	21	67	24	9	
	3 and 4 min	8	25	13	62	
		36	44	31	25	50
Intravenous gelatin 50 cc /kg 10 min to 4½ hr after injury to vein (14 dogs)	1 and 1½ min	8	25	62	13	
	2 min	32	22	13	65	
	3 min	1	0	100	0	
		41	22	24	54	73
Intravenous bovine albumin 50 cc /kg before injury to vein (10 dogs)	1 min	8	13	25	62	
	2 min	17	35	34	32	
	3 and 5 min	3	0	100	0	
		28	25	39	36	75
Intravenous physiologic saline solution 50 cc./kg before injury to vein (9 dogs)	1 min	6	50	17	33	
	2 min	22	18	14	68	
		28	25	14	61	75

amount of gelatin was given four and a half to nine hours before injury, and in the third series, 25 cc of gelatin per kilogram of body weight was given one to three hours before injury In the fourth group, gelatin was given after injury to the veins The gelatin solutions were given intravenously in a single infusion lasting from ten to twenty minutes at the rate of 15 to 20 cc a minute

Gelatin injections before injury The first series included thirty-five veins in 17 dogs Thirty veins (86 per cent) were found to be entirely patent, and

seven and nine hours before injury, nine showed complete occlusion

In the third series, the least amount of gelatin necessary to prevent clotting was investigated Twenty-five cubic centimeters per kilogram of body weight was injected one to three hours before injury to the veins Of twenty-one veins in 7 dogs exposed to injury for two minutes, fifteen remained patent and seven were partially or wholly occluded

In summary, it appears that gelatin has a definite in vivo antithrombotic effect, that when gelatin is

given prophylactically in doses of 50 cc per kilogram at intervals of one to seven hours before injury to the vein, complete occlusion rarely occurs in veins exposed for two minutes to quinine-urethane, that better protection is afforded by a single intravenous injection of 50 cc per kilogram of body weight than by one of 25 cc, and that the protective effect falls off rapidly with time but persists for as long as seven hours.

Gelatin injections after injury In the fourth series of experiments, the animals received the infusion of gelatin from ten minutes to over four hours after injury to the veins. The results obtained, as recorded in Table 2, show that only 22 per cent of the veins remained patent, 24 per cent contained small, nonoccluding thrombi, and 53 per cent were completely occluded. Hence, gelatin provides no substantial benefit when given after injury to the veins.

To test the specificity of these results, the findings following the injection of another protein solution (bovine albumin) and of physiologic saline solution were observed.

Bovine albumin solution Fifty cubic centimeters per kilogram of body weight of a 5 per cent solution of crystalline bovine albumin* was injected intravenously one to eight hours before injury to twenty-eight veins in 10 dogs (Table 2). Of the injured veins, only seven (25 per cent) were patent. The remainder showed an almost equal percentage of partial (39 per cent) and complete (36 per cent) occlusions. No definite relation appeared to exist between the incidence of thrombosis and the interval between the infusion and the injury to the veins.

Saline solution Nine dogs, in which twenty-eight veins were injured (Table 2), received intravenous infusions of physiologic saline solution (50 cc per kilogram of body weight). The injections were given forty-five minutes to four hours before the vessels were injured. Only seven (25 per cent) of the veins were completely patent. Complete venous occlusions were found in 61 per cent, and partial occlusions in 14 per cent.

Although the percentages of venous occlusion were identical in both the albumin and saline series, complete obstruction in the saline series was almost twice that of the albumin series.

Hematologic Studies

Presumably the effect of gelatin on the thrombotic process involves an alteration in the blood constituents concerned with the coagulation phenomenon. This report deals only with the hematocrit and the bleeding, clotting and prothrombin times.

Hematocrit All hematocrit determinations were made on citrated blood in Wintrobe tubes, centrifuged at a 2500 r p m for thirty minutes. Blood samples were taken at various intervals before and

after the infusion, ranging over an average period of forty-eight hours. The hematocrit did not return to its initial level within this period except in a few cases. The following is a typical example.

TIME	HEMATOCRIT
	%
Before infusion	58.0
After infusion	
5 min	34.3
1 1/4 hr	43.0
4 1/2 hr	50.5
6 1/2 hr	52.0
23 hr	50.0
50 hr	52.0

Maximal hemodilution took place within the first six hours after gelatin infusion. The return of the hematocrit to a normal value is presumably correlated to the disappearance of gelatin from the blood stream, this varies from two to five days depending on the degree of degradation of the gelatin molecule at the time of infusion.⁶

Bleeding time The normal bleeding time in dogs, determined by pricking the animal's ear, was 2 to 3 minutes. Within ten to thirty minutes after the gelatin infusion, the bleeding time was appreciably prolonged. The maximal effect was present within half an hour after the infusion, but seven hours later the bleeding time was still three or more times normal. Return to a normal level was gradual, requiring more than twenty-four hours.

Clotting time Determinations of the clotting time were made at room temperature, before and after infusion, by the Lee and White technic. The blood was withdrawn directly from the exposed vein. The average normal clotting time in these dogs was about 3 minutes. After gelatin infusion the clotting time was found to be uniformly prolonged. In some cases the clotting time twenty-four hours after infusion was still twice as long as the control value, an observation at variance with the opinion⁷⁻¹⁰ that gelatin exhibits an *in vivo* coagulant effect.

Prothrombin time The prothrombin time was determined by Quick's technic, using rabbit brain thromboplastin, on whole and on diluted plasma (25 per cent and 12.5 per cent plasma in physiologic saline solution). The prothrombin time of whole plasma after gelatin infusion was normal, but that of dilute plasma was definitely prolonged. In some cases the prothrombin time twenty-four hours after the infusion had returned to its initial values, in others it was still prolonged.

Pathological Studies†

Specimens for pathological observations were taken at four and a half hours, at twenty-four to seventy-two hours and as late as seven days after injury to the veins, in both the control and the treated series.

In the control series histologic examination in the first twenty-four hours showed the lumen of the vein

*This material was kindly supplied by Armour and Company, Chicago, having been prepared under a contract with the Office of Scientific Research and Development through the courtesy of Dr. E. J. Cohn of Harvard Medical School.

†We are indebted to Dr. Monroe J. Schlesinger, pathologist of the Beth Israel Hospital, for his help in the study of the material discussed in this section.

to be filled with a fibrin thrombus containing platelets and red cells, there were a loss of endothelium, extensive degeneration of the media, occasional engorged vasa vasorum and hyperemia. At four days the picture was much the same, the vein wall appeared distended and few signs of regeneration were seen except for a few nuclei in the media or adventitia, which again took the stain.

In the dogs treated with gelatin, the patent veins examined one to five days after the injury showed the following changes in the vascular wall. In the first twenty-four to forty-eight hours, as a rule, the cells in the various layers of the vein wall showed a loss of nuclear staining, the engorged vasa vasorum, however, were virtually intact. After five days the vein wall exhibited signs of regeneration and repair of its different layers.

The pathological data are still incomplete, especially with reference to detail in the first few hours after injury and in the successive stages of the healing process in the treated animals.

SUMMARY

An adequate technic of inducing experimental venous thrombosis in dogs has been described. The ability of gelatin to prevent such thrombosis was investigated.

Eight out of twelve samples of gelatin exhibited a definite antithrombotic action when given prophylactically in a single injection. No beneficial

effect was obtained when the gelatin was given after injury to the veins.

The bleeding time and clotting time were appreciably prolonged after gelatin infusion. The prothrombin time of whole plasma was unchanged, whereas that of diluted plasma was definitely prolonged.

These data are of a purely experimental nature and should not form a basis for clinical application until more information has been obtained.

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MEDICAL PROGRESS

GYNECOLOGY CARCINOMA OF THE ENDOMETRIUM

JOE VINCENT MEIGS, M.D.*

BOSTON

CANCER originating in the endometrial lining of the uterus has been given varied nomenclatures, such as "cancer of the fundus," "cancer of the body," "cancer of the uterus" and "cancer of the endometrium." Inasmuch as this tumor arises from the cells of the endometrium, it is proper to speak of it as cancer of the endometrium. This tumor is not so frequent as is carcinoma of the cervix, and, until far advanced, it is not nearly so lethal. At the Pondville Hospital since 1927 there have been approximately 1500 cases of cervical cancer and 300 cases of endometrial cancer, a ratio of 5:1. Watkins and Neilson¹ report 216 cases of cancer of the cervix and 43 of cancer of the endometrium, an identical ratio. Masson,² of the Mayo Clinic, writes that of 4407 cases of cancer of the uterus in their institution 3273 were of the cervix and 1134

of the endometrium, a ratio of about 3:1. There is a marked difference between the material from public hospitals and that from private practice. The number of cervical cancers is greater among the poor, and endometrial cancer is more frequently encountered in private practice. It is quite possible that, although clinic patients receive excellent obstetric care at the time of delivery, during follow-up the care of the cervix is not so complete and thorough as in the practice of the private obstetrician. This difference possibly explains the comparative absence of cervical cancer in private offices. There are of course differences in diet, hygiene and so forth that could be responsible, but the most obvious contrast lies in the more perfect care of the cervix of the private patient after delivery. Cancer of the endometrium is in most cases a comparatively mild type of tumor, but it can be extremely malignant and rapidly growing. Usually it is nonfatal while within

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given prophylactically in doses of 50 cc per kilogram at intervals of one to seven hours before injury to the vein, complete occlusion rarely occurs in veins exposed for two minutes to quinine-urethane, that better protection is afforded by a single intravenous injection of 50 cc per kilogram of body weight than by one of 25 cc, and that the protective effect falls off rapidly with time but persists for as long as seven hours.

Gelatin injections after injury In the fourth series of experiments, the animals received the infusion of gelatin from ten minutes to over four hours after injury to the veins. The results obtained, as recorded in Table 2, show that only 22 per cent of the veins remained patent, 24 per cent contained small, nonoccluding thrombi, and 53 per cent were completely occluded. Hence, gelatin provides no substantial benefit when given after injury to the veins.

To test the specificity of these results, the findings following the injection of another protein solution (bovine albumin) and of physiologic saline solution were observed.

Bovine albumin solution Fifty cubic centimeters per kilogram of body weight of a 5 per cent solution of crystalline bovine albumin* was injected intravenously one to eight hours before injury to twenty-eight veins in 10 dogs (Table 2). Of the injured veins, only seven (25 per cent) were patent. The remainder showed an almost equal percentage of partial (39 per cent) and complete (36 per cent) occlusions. No definite relation appeared to exist between the incidence of thrombosis and the interval between the infusion and the injury to the veins.

Saline solution Nine dogs, in which twenty-eight veins were injured (Table 2), received intravenous infusions of physiologic saline solution (50 cc per kilogram of body weight). The injections were given forty-five minutes to four hours before the vessels were injured. Only seven (25 per cent) of the veins were completely patent. Complete venous occlusions were found in 61 per cent, and partial occlusions in 14 per cent.

Although the percentages of venous occlusion were identical in both the albumin and saline series, complete obstruction in the saline series was almost twice that of the albumin series.

Hematologic Studies

Presumably the effect of gelatin on the thrombotic process involves an alteration in the blood constituents concerned with the coagulation phenomenon. This report deals only with the hematocrit and the bleeding, clotting and prothrombin times.

Hematocrit All hematocrit determinations were made on citrated blood in Wintrobe tubes, centrifuged at a 2500 r p m for thirty minutes. Blood samples were taken at various intervals before and

after the infusion, ranging over an average period of forty-eight hours. The hematocrit did not return to its initial level within this period except in a few cases. The following is a typical example.

TIME	HEMATOCRIT
	%
Before infusion	58.0
After infusion	-
5 min	34.3
1 1/2 hr	43.0
4 1/2 hr	50.5
6 1/2 hr	52.0
23 hr	50.0
50 hr	52.0

Maximal hemodilution took place within the first six hours after gelatin infusion. The return of the hematocrit to a normal value is presumably correlated to the disappearance of gelatin from the blood stream, this varies from two to five days depending on the degree of degradation of the gelatin molecule at the time of infusion.⁶

Bleeding time The normal bleeding time in dogs, determined by pricking the animal's ear, was 2 to 3 minutes. Within ten to thirty minutes after the gelatin infusion, the bleeding time was appreciably prolonged. The maximal effect was present within half an hour after the infusion, but seven hours later the bleeding time was still three or more times normal. Return to a normal level was gradual, requiring more than twenty-four hours.

Clotting time Determinations of the clotting time were made at room temperature, before and after infusion, by the Lee and White technic. The blood was withdrawn directly from the exposed vein. The average normal clotting time in these dogs was about 3 minutes. After gelatin infusion the clotting time was found to be uniformly prolonged. In some cases the clotting time twenty-four hours after infusion was still twice as long as the control value, an observation at variance with the opinion⁷⁻¹⁰ that gelatin exhibits an *in vivo* coagulant effect.

Prothrombin time The prothrombin time was determined by Quick's technic, using rabbit brain thromboplastin, on whole and on diluted plasma (25 per cent and 12.5 per cent plasma in physiologic saline solution). The prothrombin time of whole plasma after gelatin infusion was normal, but that of dilute plasma was definitely prolonged. In some cases the prothrombin time twenty-four hours after the infusion had returned to its initial values, in others it was still prolonged.

Pathological Studies†

Specimens for pathological observations were taken at four and a half hours, at twenty-four to seventy-two hours and as late as seven days after injury to the veins, in both the control and the treated series.

In the control series histologic examination in the first twenty-four hours showed the lumen of the vein

*This material was kindly supplied by Armour and Company, Chicago, having been prepared under a contract with the Office of Scientific Research and Development through the courtesy of Dr. E. J. Cohn of Harvard Medical School.

†We are indebted to Dr. Monroe J. Schlesinger, pathologist of the Beth Israel Hospital, for his help in the study of the material discussed in this section.

other etiologic factor should be clarified. It is well substantiated that cancer of the cervix is frequently found in women who have borne many children, whereas in endometrial cancer the reverse is apt to be true. Barns⁸ concludes that multiparas and primiparas are involved in equal numbers but that endometrial cancer comes in the unused organ and cervical cancer in the used. Radium or x-ray treatment as a reason for the occurrence of such growths must be considered. Luker¹² reports a case of his own and points out 14 others in the literature. There is no doubt that radiation may form the base of an epithelioma, for it often occurs on the skin following radiation treatment. Injury of the endometrium due to radium in the uterus may constitute the nidus of an epithelial growth, yet in many of the cases reported by Luker, the tumors came so soon after the radium treatment as to make one think that the tumor was present at the time of the curettage and was missed by the curette. Scheffey¹³ collected from the literature 71 cases of cancer following radiation, in 18 the cervix was affected, in 40 the endometrium, and in 13 the location was not stated. He added 20 cases — 7 of cancer of the cervix, 12 of cancer of the endometrium and 1 of myosarcoma. From his analysis of these cases he concludes that errors of omission in either technic or judgment and not the radiation therapy itself were the responsible factors in the subsequent occurrence of cancer. Randall,¹¹ however, reports 4 such cases a year after treatment with 1000 to 1800 mg hr of radium. Corscaden¹¹ in discussing Randall's paper states his belief that the radiation menopause has no therapeutic value in preventing cancer, but he doubts that it is a cause of cancer. He thinks that intra-uterine radium may be a cause of cancer in the uterine cavity, just as it may produce cancer on an epithelial surface in other parts of the body. Cancer of the cervix or upper vagina occurring five to ten years after previous proper treatment of a cervical cancer may be a recurrence or it may be due to the radium treatment itself, and the same applies to cancer of the endometrium.

The question of whether estrin is a responsible etiologic factor in the development of endometrial cancer has not been decided. It is the opinion of most gynecologists that treatment of the menopause in cases with the uterus intact should be carefully thought out, that the dosage of estrin should be small, that the drug should be withheld one week out of every month and that, if withdrawal bleeding occurs two weeks later, curettage should be performed. All authorities admit that estrin is a potent growth-producer and that in certain types of animals one can produce cervical and endometrial cancer. Important evidence is furnished by the facts that Smith¹⁴ has found thecal-cell hyperplasia in a number of cases of cancer of the endometrium, that I have recently observed it in the ovaries of a patient with cancer of the cervix and that many have noted

the frequency with which adenocarcinoma of the endometrium is present in patients with granulosa-cell or thecal-cell cancers of the ovary.

Most observers have rarely seen cancer of the endometrium in the castrated. Ingraham, Black and Rutledge¹⁵ note that Dr G Van S Smith has reported 3 cases of cancer of the endometrium occurring fifteen years after bilateral oophorectomy. The facts mentioned concerning fibroids, cancer and bleeding at the menopause, and also the fact that Randall¹¹ has noted the infrequency of hot flashes and atrophy in women with endometrial cancer, are significant. I have noted the absence of hot flashes in patients with cervical cancer who have received radiation. All these findings should make one hesitate to give estrin or diethylstilbestrol to every patient with a complaint, whether or not it can be attributed to the menopause. Ladin¹⁶ warns that it is not to be taken for granted that bleeding in the treatment of the menopause is due to estrin. Without confirmation by curettage, Scheffey, Farell and Hahn¹⁷ say that when abnormal bleeding is present during the later reproductive, menopausal and post-menopausal periods there is much less justification for prolonged endocrine therapy. They report cases in which endocrine therapy was introduced to control abnormal bleeding without preliminary examination to exclude organic pelvic disease, the result being a delayed diagnosis and treatment of uterine cancer. Corscaden, in discussing the above paper, states his belief that there is a relation between estrogen stimulation and the later development of cancer.

Ingraham, Black and Rutledge¹⁵ quote Dockerty as reporting 3 cases of cancer of the endometrium in 32 cases of granulosa-cell tumor and 1 in 10 cases of thecal-cell tumor, and conclude that the incidence of 10 per cent is more than coincidental. They themselves report 2 cases of endometrial cancer in granulosa-cell tumor and 1 in thecal-cell tumor of the ovary. In the discussion of this paper Stohr reports the case of a patient with cancer of the endometrium who simply had her granulosa-cell tumor removed and who on subsequent curettage had no cancer. Hertig¹⁸ states that at the Free Hospital for Women (Brookline, Massachusetts) at least 18 to 20 per cent of the patients with granulosa-cell tumors and thecomas have an associated carcinoma of the endometrium.

Novak¹⁹ reports a case in which a diagnosis of cancer of the endometrium was made following estrogenic treatment but in which subsequent curettage after cessation of treatment showed no cancer. Ingersoll²⁰ curetted a patient who had bled following estrogen treatment and the pathologist reported carcinoma of the endometrium, a subsequent curettage two weeks later showed no cancer and intrauterine radium treatment was given, six weeks later the uterus was removed and no cancer was found. Novak¹⁹ advises against prolonged and

the confines of the uterus itself but becomes fatal once it has grown beyond the walls of that organ

ETIOLOGY

The etiology of nearly all forms of cancer is still one of the great mysteries of the human body, and there is no evident cause for this particular type of growth. There have been many attempts to explain the presence of endometrial cancer and many suggestions to this end have been made, but none have thus far proved satisfactory. The late Dr. William P. Graves believed that endometrial cancer and possibly endocervical cancer was due to the irritation of retained secretions, owing to stenosis of the cervix. He thought that poor drainage caused by old cervical scars or cervical atrophy produced a definite irritation and chronic inflammation, and hence cancer. Chronic irritation, together with other factors, may easily have something to do with the formation of cancer. It is not infrequent that pyometrium is noted along with endometrial cancer, and the retention of pus, even though sterile, is almost certain to cause a severe irritation within the uterine cavity. On the other hand, pyometrium is often found in patients with cancer of the cervix and not infrequently in those whose cervical cancer has been treated with radium, yet cancer of the endometrium in these two conditions is extremely infrequent.

It is certain that chronic irritation is not the only cause of this type of cancer, although it is unquestionably present in some. It has been supposed that endometrial cancers may arise on a basis of endometrial polyps, just as intestinal cancer is so frequently found in patients with intestinal polyps. Hirson³ reported 4 cases in which polyps were found coincidentally with cancer of the endometrium or in which they had previously been removed. Ferris and Dockerty⁴ report such a case, and they discuss the criteria for determining that a cancer arises in a polyp: the carcinoma must be confined to one portion of the polyp, the base of the polyp must be benign, and the surface of the endometrium around the base of the polyp must show no malignant change. Their case fulfilled these criteria and must be accepted as a true adenocarcinoma in an endometrial polyp. It may be that other malignant polyps have been found, but it is certainly true that most endometrial polyps are benign and that most cancers of the endometrium do not arise in polyps. The supposed analogy to cancer of the large bowel is not a true one.

Frequently fibroids have been regarded as contributing in some way to the etiology of endometrial cancer. There is no doubt that fibroids are often encountered in patients with endometrial cancer, but by far the vast majority of them seem to have no relation to cancer. If fibroids are due to some abnormality in the reaction of estrin and its sister hormones, the possibility of an association is definite,

but a fibroid alone is not an etiologic factor. Masson and Gregg⁵ in a series of 590 patients who had been operated on found that 36 per cent also had fibroids. Miller⁶ found them in 20 per cent of his cases. Adair⁷ believes that 2 per cent of patients with uteruses containing fibroids have an accompanying cancer of the uterus and that 38 per cent of patients with cancer of the endometrium have fibroids. Barns⁸ found fibroids in 24 per cent. Watkins and Neilson¹ report fibroids in 38 per cent of their cases of cancer of the endometrium and believe that in some way these tumors are an etiologic factor. Healy⁹ found 40 per cent of his surgically treated patients with endometrial cancer also had fibroids, and thinks of this as more than a coincidence, believing that the presence of fibroids indicates that the uterus has tumor-growing possibilities. He advocates removal of the uterus in patients with fibroids over 5 cm in diameter. Scheffey, Thudium and Farrell¹⁰ found fibroids in 38 per cent of all patients treated surgically. Randall¹¹ believes that the consensus at the present time is that cancer of the endometrium develops just as frequently in a nonfibroid as in a fibroid uterus, and that the presence of a fibroid does not predispose to the development of cancer of the endometrium. His figures substantiate this. If one admits, however, that fibroids are in some way a development of abnormally functioning hormones, — as many surgeons do, — and if one looks at the results of Randall's excellent investigations, one is drawn toward the idea that uterine growths, including fibroids, are the effect of some fundamental disturbance that is also present in the formation of cancer of the endometrium.

Randall shows that patients with menorrhagia at the time of the menopause are three and a half times likelier to develop cancer of the endometrium later than are those who have an uneventful cessation of periods. His figures also show that only 8 per cent of women who did not develop cancer flowed beyond the age of fifty, whereas 35 per cent of those with endometrial cancer did so after fifty-one. No doubt many of these women had fibroids and therefore bled abnormally. He also states that many women with endometrial cancer have not had hot flashes, and do not have vulvar atrophy or senile changes of the vagina. He believes that there is a definite connection between granulosa-cell or thecal-cell tumors of the ovary — both of which produce estrin — and the presence of endometrial cancer. The last phenomenon has been noted by many authors.

All these findings considered together lead one to conclude that fibroids may not be an etiologic factor, but that they and endometrial cancers are produced just as are abnormal bleeding at the menopause and hyperplasia of the endometrium.

Before the evidence for and against a hormonal etiology of this cancer is given, the question of any

ment and who sixteen years later had the same type of tumor. These cases indicate the slow growth of some of the endometrial cancers, but there is always a question whether such patients had cancer or merely atypical hyperplasia.

PATHOLOGIC HISTOLOGY

Cancers of the endometrium are divided by some authors into adenoma malignum and adenocarcinoma. Grades I, II and III. Many omit adenoma malignum and believe that it really represents a Grade I adenocarcinoma. It is my belief that there is no such thing as adenoma malignum and that this nomenclature should be discarded. There is another epithelial tumor of the endometrium that is not often mentioned, namely, adenoacanthoma. This tumor is a combination of malignant adenocarcinoma and malignant squamous-cell carcinoma. It may occur in the endocervix and cervix, as well as in the endometrial cavity. Its treatment is the same as that for any cancer of the endometrium, except that it should never be treated with radium alone, since the results from such treatment are poor. Healy and Brown³⁶ believe that approximately half the endometrial cancers are adenoma malignum, one quarter adenocarcinoma, Grade II, and one quarter adenocarcinoma, Grades III and IV. Miller⁶ thinks that histologic grading helps in the prognosis but is only one of several factors, he is not impressed with the fact that Grades I and II are radiation-resistant. Corscaden³⁷ believes that tumor grading is less important in radiation cases than in hysterectomy cases. The pathologic histology of these tumors is important only in that they can be distinguished as slowly, moderately fast and rapidly growing tumors and as a combination of adenocarcinoma and squamous-cell carcinoma.

Carcinoma simplex is also reported, but this tumor may be simply an adenocarcinoma growing so rapidly that it is impossible for it to differentiate. Epidermoid cancer of the endometrium is found and probably arises in areas of metaplasia. Such areas are occasionally found in the normal uterus, and it is not difficult to believe that epidermoid cancer might originate in such an area.

SYMPTOMS

The chief symptoms of endometrial cancer are bleeding, discharge and pain. The bleeding may be profuse in the premenopausal period or at the time of catamenia, in the postmenopausal stage, the bleeding is often fairly continuous and small in amount. The discharge is watery and tinged with blood, both before and after the menopause. Pain indicates extension of disease and usually means a poor prognosis. Most patients with cancer of the uterus are in the postmenopausal age group, the

most frequent age period being fifty to fifty-nine. Kamniker³⁵ states that he did not find a single patient under thirty. Scheffey, Thudium and Farell¹⁰ assert that bleeding is the most significant symptom, having been present in 96 per cent of their series. Corscaden³⁹ found that of 201 patients one third had symptoms for more than one year and half for more than six months before the patients first went to their physicians.

DIAGNOSIS

The diagnosis is made on microscopic examination of the endometrium, either after the uterus is removed or after curettage. The removal of small specimens with the endometrial biopsy curette is not a satisfactory method of making the diagnosis. If the piece of tumor removed shows cancer, the diagnosis is made, but a negative report is not convincing. Ward⁴⁰ believes that diagnostic dilatation and curettage is the most valuable method of making the diagnosis and that early diagnosis is essential. Ladin¹⁶ states that in 1914 he reported 3 cases of cancer of the endometrium cured by curettage alone. Previous to his report 18 cases had been reported, and he therefore advises dilatation and curettage previous to operation. If there is a question concerning the presence of cancer in a given specimen, one should not rely on a frozen section but should wait until the tumor has been properly cut and studied. He is opposed to vaginal hysterectomy when cancer is suspected. MacFarlane, Sturgis and Fetterman⁴¹ report an early case in their yearly examination clinic in which the patient was well six years after radium and x-ray treatment, and one in which the patient after the seventh visit was found to have a symptomless fibroid and was operated on elsewhere by supravaginal hysterectomy, a small tumor being found just above the line of removal. The latter patient was well two years later. Supravaginal hysterectomy is not the proper treatment for cancer of the endometrium.

The history and a curettage were the only ways to make a diagnosis of carcinoma of the endometrium before operation until Papanicolaou and Traut⁴² in 1941 and Meigs, Graham, Fremont-Smith, Kapnick and Rawson⁴³ in 1943 demonstrated the practicability of vaginal smears in the diagnosis. Vaginal-smear diagnosis in carcinoma of the endometrium is not so accurate as that in cancer of the cervix. There is no question that the cells exfoliate, but diagnosis from the cells is more difficult. The best percentage of correct diagnosis by this method is between 80 and 85 per cent. According to Papanicolaou and Marchetti,⁴⁴ Bourgeois and Carv advised removing material for smears from the uterus by means of a suction apparatus, the former agree that this method has great possibilities. The use of the method of vaginal smears described by Papanicolaou will become of increas-

excessive treatment with estrogens after the cessation of ovarian function because of the frequent finding of endometrial hyperplasia and cancer. Crossen and Hobbs²¹ found that 60 per cent of women with uterine cancer still continue to menstruate after the age of fifty, whereas in a large number of women without uterine cancer menstruation occurs at this late age in only 15 per cent. According to an editorial in the *Journal of the American Medical Association*,²² these findings suggest that the long-continued action of ovarian hormones may be of significance in the origin of cancer not only of the mammary glands, the cervix and the vagina but also of the fundus of the uterus. Crossen and Loeb,²³ however, state that hormones alone are not responsible and that other factors must be present along with growth-producing factors. Randall¹¹ writes that Herrell studied the blood estrogens in women with cancer of the uterus in the postmenopausal period and reported no significant high levels. It is agreed, however, that the cause of hyperplasia of the endometrium is persistent, not high, levels of estrin. Jones and Brewer²⁴ found that of 19 premenopause patients with cancer of the endometrium 11 had cyclic menstruation, and of 9 operated on 8 had functioning corpora lutea. The ovaries may function normally and part of the endometrium may be normal. They believe that cystic changes in the ovaries are incidental and without significance.

From all this material it is evident that the estrins and similar preparations may be indicted in tumor production in both animals and human beings. Definite cancer production in the latter has not been proved, but there is enough suggestion of it to make one careful of excessive and prolonged treatment with estrin. Cancer of the endometrium does occur in patients before the menopause. Wallis²⁵ reports that Stacey found 36 per cent of his patients to be in the premenopausal stage, Norris and Dunne 30 per cent, and Masson and Gregg 33 per cent.

Cancer of the endometrium spreads by way of the lymphatics and blood vessels and possibly by the vertebral system of veins, as described by Batson.²⁶ The nodes involved are apt to be higher than those involved in cervical cancer—usually the upper iliac and lumbar nodes or those in the neighborhood of the kidneys. The vagina, the tubes and the ovaries are also attacked. The involvement of any of these organs makes for an extremely poor prognosis. Johnston²⁷ has advocated dissection and removal of the common iliac, uterine and external iliac nodes in doing a hysterectomy for cancer of the endometrium, but in my opinion this sort of procedure should accompany the operation for cancer of the cervix rather than that for endometrial cancer. Vaginal extensions have been noted by Strachan,²⁸ who believes that surface spread or submucous lymphatic infiltration is rare; he found vaginal metastases only in cases that were far advanced. In 90 cases, vaginal implants were noted in 12 and

no patient survived. I²⁹ found that vaginal metastases were not infrequent, noting them in 25 (12 per cent) of 206 cases at the Huntington Memorial Hospital. I believe that the extension is not an implantation but is a lymphatic metastasis by way of the cervix, which has a lymphatic connection with the uterus. This form of metastasis may be spread during hysterectomy, either by implantation in the raw vaginal cuff or by pressure on the lymphatics of the fundus. At the Pondville Hospital, radium treatment is given before operation, which is performed six weeks later, and in seven years there has been no case with a vaginal metastasis. The prognosis of patients with vaginal metastases is poor.

Involvement of the fallopian tubes and their role as paths of extension for cancer of the uterus to the ovary and cancer of the ovary to the uterus are discussed by Wallis²⁵ and by Lynch and Dockerty.³⁰ All these authors agree that cancer is found in the lumen of the tubes both free and implanted. Philipp and Huber³¹ report that in 16 of 62 patients they found extension into the tube. In 9 cases the tumor was free in the tube, and in 1 it was found on the surface of the ovary. Over twenty-six years ago Sampson³² advocated tying the ends of the tubes as the first step in hysterectomy, and also avoiding dilatation and curettage to prevent forcing cancer cells out through the tubes. Gentle manipulation of the uterus at examination in patients with suspected cancer of the endometrium is universally advised. Lynch and Dockerty³⁰ believe that the tubes are rarely the pathway of cancer extending to the ovaries or peritoneal cavity, but admit that this is possible. They conclude from anatomical studies that it is likelier that extension takes place by way of the lymphatics or by direct extension.

Involvement of the ovaries by cancer of the endometrium is a definite possibility, and in many hands these cases have done poorly. Barns³³ has reported that 7 of 95 patients had such involvement, and he believes that the prognosis is good, provided that there is no other extrauterine extension. This has not been my experience. Lynch and Dockerty³⁰ found that in 4 per cent of the operated cases of cancer of the endometrium one or both ovaries were eventually involved with cancer.

Brezina and Lindskog³⁴ report a total pneumonectomy for discrete tumor of the upper lobe of the right lung following hysterectomy for cancer of the endometrium, with removal of both tubes and ovaries, some years before. The patient recovered, and the tumor proved to be a metastasis from the cancer of the endometrium.

Barrows³⁵ operated on a patient with cancer of the endometrium who was given radium nine and four years before hysterectomy and who subsequently lived for six years in good health. Taylor, in discussing the paper, reported a patient who had had a dilatation and curettage for adenoma malignum at the age of forty-five, who had had no treat-

pregnancy and there is no extension, the five-year cures should be 60 per cent. Their five-year cures for 96 patients who could not undergo hysterectomy and were treated with radium was 39 per cent. It is therefore evident that five-year cures of at least 60 per cent should be obtained in the combined treatment of this disease.

CONCLUSIONS

Cancer of the endometrium is curable in a large percentage of cases.

The proper treatment consists of radium or x-ray or both, followed by total hysterectomy and bilateral salpingo-oophorectomy, with the removal of a large vaginal cuff, if possible.

Dissection of the lymph nodes has not as yet proved its value, but may do so in the future.

The diagnosis is best made by curettage, endometrial biopsy is not satisfactory.

Estrin in some form is possibly one of the etiologic factors. Endometrial polyps, unlike intestinal polyps, are probably not frequent etiologic factors.

The pathologic diagnosis of adenoma malignum should be discarded.

Cancer of the endometrium is extremely malignant once it has grown beyond the confines of the uterus.

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ing value to clinicians as more and more laboratories are equipped to carry out proper interpretation of the slides

TREATMENT

Treatment of cancer of the endometrium may be surgical or radiologic or a combination of both. There is no doubt that nearly all workers in this field believe that the combination treatment is the most satisfactory. Thus, of sixteen writers on the subject, all but two agree that the results are better with the use of radiation and surgery. Three have employed vaginal hysterectomy to a large extent, and one of these always removes the ovaries at the time of the operation. Some prefer to use radiation exclusively, and all admit that good results can be obtained if it is properly given. Masson,² with the largest series, gives his immediate mortality for total hysterectomy in cases of endometrial cancer as 4.5 per cent, that for vaginal hysterectomy as 3.2 per cent, and that for subtotal hysterectomy as 9.2 per cent and that for radiation as 1.5 per cent. Healy and Brown³⁶ advocate not less than 3600 mc hr of intrauterine radium before operation and believe that 75 per cent of the patients so treated should survive for five years. Philipp and Huber³¹ prefer vaginal hysterectomy. All agree that the operative mortality following total hysterectomy should not exceed 2 per cent. Arneson⁴⁵ advises x-ray and radium for the operable group and x-ray and radium as for cancer of the cervix in the inoperable group. Crossen⁴⁶ believes that preliminary radiation decreases the chance of metastasis. He distributes the radium along a special wire apparatus or packs it in with detached units. Miller⁶ advises proper radiation, followed by total hysterectomy six weeks later. Johnston²⁷ recommends removal of the regional lymph nodes in addition to total hysterectomy. Kennedy⁴⁷ has never had a recurrence of cancer following vaginal hysterectomy by the clamp method when there was no involvement of the peritoneal coat at the time of operation. He speaks strongly against dilatation and curettage. Schmitz, Sheehan and Towne⁴⁸ found that of 11 patients receiving hysterectomy after full radium treatment 5 were free of cancer. Corscaden^{37, 39} believes that there is a chance for improvement in the method of radium application and in the order in which radium, x-ray and surgery are given. He thinks that 60 per cent of the patients operated on today should survive five years. He quotes Heyman as having consistently improved his percentage of cures until in his 1932-1935 group it was 63 per cent. Corscaden obtains some relief from the use of x-ray in pelvic and abdominal-wall extensions. He thinks that the combined treatment should give 80 per cent five-year cures. In his radiated cases 24 per cent showed no cancer when the uterus was removed. He quotes Farras as having 6 of 27 patients without cancer after radium,

Donovan and Warren 5 of 46, Martin 3 of 4 and Schmitz, Sheehan and Towne 4 of 5. Corscaden was able to keep 55 per cent of his patients well for five years with radium alone.

At the Pondville Hospital the uterus is measured with a hysterometer, and a gold radon tube is made that fits into a Monel applicator of the same measurement as the uterus. This is left in the uterine cavity long enough to give 3500 mc hr of radiation, and is followed by x-ray therapy, if desired. Total hysterectomy is done six weeks later. In few cases has all the cancer disappeared. In most cases the tumor shows marked injury and no vaginal metastases have occurred. It might be argued that six weeks' delay after radiation is too long a time, but with this delay no cancer had advanced beyond what it was before radiation was given, and usually the uterus is definitely smaller. In a few cases evidence of radiation reaction is found on the outside of the uterus or on the surface of the intestine, but no disaster has occurred since its use. Operation is no more difficult in those cases than in those in which radiation has not been given. If technically possible, a good-sized vaginal cuff should be removed. Both tubes and ovaries should always be removed. The dissection of the lymph nodes is not advocated at present, but after it has been done in more cases and the results have been reported it may easily become a part of the operation. For the inoperable cases x-ray and radium in full doses should be given. Great care should be taken to spread the radiation throughout the whole uterine cavity, for every part of it must be radiated if success is to follow.

The results of treatment vary. Arneson⁴⁵ found that the average five-year cures from surgery were 55 to 60 per cent and those from radiation in favorable cases 50 to 55 per cent. Miller,⁶ treating inoperable cases with x-ray and radium, kept 34 per cent of the patients well for five years. In the operable group his results from radium and total hysterectomy were 71 per cent cures for five years. Masson and Gregg⁵ effected cures for five years in 60 per cent of 711 cases and cures for ten years in 48 per cent of 520 cases. Smith¹⁴ reports 58 per cent of 307 cases cured for five years and 45 per cent for ten years. He believes that if a patient survives thirteen years after treatment of this disease, she is cured. Scheffey, Thudium and Farell¹⁰ effected five-year cures in 36 per cent of patients with surgery alone, in 41 per cent with radiation alone and in 38 per cent with surgery and radium. Corscaden³⁷ found that if the uterus was smaller than an eight-week pregnancy his results were 75 per cent cures for five years, a large uterus giving but 37 per cent results, and that if the cancer was beyond the uterus only 5 per cent of the patients survived five years. Healy and Brown³⁶ believe that adenoma malignum or low-grade cancer and adenocarcinoma give about the same results. If the uterus is not larger than a two-and-a-half-month

pregnancy and there is no extension, the five-year cures should be 60 per cent. Their five-year cures for 96 patients who could not undergo hysterectomy and were treated with radium was 39 per cent. It is therefore evident that five-year cures of at least 60 per cent should be obtained in the combined treatment of this disease.

CONCLUSIONS

Cancer of the endometrium is curable in a large percentage of cases.

The proper treatment consists of radium or x-ray or both, followed by total hysterectomy and bilateral salpingo-oophorectomy, with the removal of a large vaginal cuff, if possible.

Dissection of the lymph nodes has not as yet proved its value, but may do so in the future.

The diagnosis is best made by curettage, endometrial biopsy is not satisfactory.

Estrin in some form is possibly one of the etiologic factors. Endometrial polyps, unlike intestinal polyps, are probably not frequent etiologic factors.

The pathologic diagnosis of adenoma malignum should be discarded.

Cancer of the endometrium is extremely malignant once it has grown beyond the confines of the uterus.

264 Beacon Street

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor**

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CASE 31271

PRESENTATION OF CASE

A sixty-five-year-old man was admitted to the hospital because of progressive malaise, anorexia, weakness, weight loss and swelling of the ankles.

The patient had been well and active as a shoemaker until about nine months before admission, when because of malaise and loss of strength he went to a physician. The patient was referred to a thoracic surgeon but failed to seek further medical aid until seven months later. Beginning nine months before admission the tips of the fingers and toes were observed to have become progressively larger. There had been no chest pain, cough, dyspnea or fever. He had experienced periods of pain in the fingers, elbows, hips, knees and ankles over this period. The ankles had swollen progressively since the onset of his illness and caused the most frequent joint pain. The knees became swollen on occasion. Aspirin brought considerable relief, but the taking of these tablets was followed by night sweats. His normal weight was about 125 pounds, and on admission he weighed 105 pounds.

Over the fifteen years before admission he had had vague joint pains that responded to aspirin, but these were unlike the pains experienced during the nine months before entry.

Physical examination revealed a well developed, pale, somewhat wasted and drawn man who was alert, co-operative and in no distress. The superficial veins were prominent over the entire body but were not distended. No superficial lymph nodes were felt. There was marked clubbing of the fingers and toes. There was moderate nonpitting edema of the ankles and feet bilaterally. The chest was symmetrical, with good expansion. The neck was normal. The lungs showed slight dullness to percussion and an area of tubular breathing at the right base posteriorly. There was a small area of dullness and diminished tactile fremitus over the left apex posteriorly. A few fine high-pitched rales were heard at the left posterior base. The heart and abdomen were normal, the liver and spleen not being palpable. A small right direct inguinal hernia was present. The joints of the hands, arms and legs were not enlarged

and showed no limitation of motion. The ankles were not red or hot.

The temperature was 100.0°F, the pulse 80, and the respirations 24. The blood pressure was 110 systolic, 60 diastolic.

Examination of the blood showed a white-cell count of 13,000, with 73 per cent neutrophils. The hemoglobin was 11.0 gm. The urine was normal but for an occasional red and white cell in the sediment. The serum nonprotein nitrogen was normal. The protein was 6.5 gm per 100 cc, the albumin-globulin ratio 1.2, the phosphorus 5.3 mg per 100 cc, the chloride 91 milliequiv per liter, the acid phosphatase 3.8 units per 100 cc, and the prothrombin time 36 seconds (normal, 18 to 20 seconds).

X-ray examination of the chest revealed a 10-by-9-by-9-cm shadow of increased density in the posterior portion of the base of the right lower lobe (Fig 1). The shadow appeared to be fairly homogeneous in density. An additional shadow measuring 3 by 2 cm was seen overlying the right third rib laterally. The remainder of the lung fields was clear. The diaphragm was low, and the right half showed some limitation in motion. The bones of the chest appeared normal. Fluoroscopy and Bucky films showed the mass in the right lower chest to move with the lung rather than with the ribs and over a fairly large portion of its circumference it was possible to see what appeared to be the inner surface of a wall. The smaller mass was not seen by fluoroscopy. An intravenous pyelogram was negative. Anechinococcus antigen skin test was negative. X-ray examination of the hands and feet showed extensive periosteal proliferation involving the distal extremities of the radius, ulna, tibia and fibula on both sides and several metatarsals and metacarpals.

After the first week the patient ran a low-grade fever. The clinical picture showed no further change. On the fifteenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR ARTHUR J LINENTHAL. The discussion of this case seems to divide itself into two parts: the first is concerned with the primary diagnosis of what was obviously a tumor inside the chest, and the second with the associated hypertrophic osteoarthropathy and clubbing of the fingers, which the patient had to a striking degree.

Hypertrophic osteoarthropathy is apparently a disease similar in character to the process that leads to clubbing of the fingers, although it involves the more proximal joints of the extremities and gets its name from the fact that there are hypertrophic changes in the bone and disturbances in the joints. The symptoms of the hypertrophic osteoarthropathy that this patient manifested were somewhat more striking than what are usually seen. He had pain involving many of the joints. This pain was presumably much severer than the vague joint pains

*On leave of absence

that he had previously had. The joints themselves were not unusual on physical examination. There was no limitation of motion, no evidence of fluid, and in the ankles, where he had had the most trouble, there was absolutely no evidence of any acute process. He had moderate nonpitting edema of the feet and ankles. This apparently was not due to a collection of fluid, or it would have pitted, but undoubtedly was a manifestation of the hypertrophic changes in the soft tissue that are sometimes seen

DR GEORGE W. HOLMES: The striking thing in the films is the large, round, sharply defined tumor in the chest. The fact that the tumor is so round and smooth and so homogeneous in density puts it in a fairly definite group. I think it would be unlikely for a malignant tumor to reach that size and be as round and sharp. There is no evidence of interference with air flow in or out of the bronchi, and no evidence of involvement of the pleura. The tumor lies posteriorly, as you can see in the lateral



FIGURE 1 Roentgenogram of the Chest

Note the large round lesion in the lower portion of the right chest and the small lesion (arrow) over the right third rib

in this syndrome. The most striking feature of the osteoarthropathy is apparent in the x-ray films.

Clubbing of the fingers and hypertrophic osteoarthropathy can be seen in a great many conditions, but certainly the most frequent association is with diseases of the lung or related structures inside the chest, and undoubtedly that was the association in this case. As a matter of fact, the patient first went to a doctor, not because of pulmonary symptoms, but because of generalized symptoms of malaise, loss of appetite, weakness and weight loss, and at no time during his illness did he have any symptoms referable to the chest.

view. It would be interesting to speculate whether it contained fat. Dermoid cysts contain fat, and sometimes this can be shown by x-ray. I should say that this tumor does not show any evidence of fat.

The films of the leg and wrist show the characteristic appearance of pulmonary osteoarthropathy; in these cases these changes are the most striking near the ends of the bones.

DR LINENTHAL: What can be said about the small shadow in the upper part of the right chest?

DR HOLMES: I do not know what it is.

DR LINENTHAL: Could it be a metastatic lesion?

DR HOLMES: In other words, you would like to

think that they are both part of the same process and that the large tumor is also a metastasis?

DR LINENTHAL Could the smaller lesion be an unrelated metastasis from somewhere else?

DR HOLMES I question whether the large shadow could be a metastasis because of its size. The only tumors that metastasize like that are the sarcomas, and there is no evidence in this story that the patient had sarcoma elsewhere in the body.

DR LINENTHAL How much significance can be attached to the statement in the fluoroscopic note that it was possible to see the inside of the wall of the mass?

DR HOLMES They were speculating whether this was a cystic or a solid tumor. There are several ways of determining that information, none of which are particularly accurate. If you can see the inside of the wall, that usually means that the tumor is cystic. Sometimes it changes shape on respiration, and that is evidence that it is cystic. Both observations have to be taken with a grain of salt.

DR LINENTHAL We have then a large tumor in the chest, and the problem is to decide the nature of this tumor. There appear to be several possibilities. First is the question whether it arose from the chest wall. The observation on fluoroscopy that the tumor moved with the lung and not with the chest wall tends to rule out that possibility. Similarly, as Dr Holmes points out, there was no involvement of the pleura.

The second question is whether it was a primary lung tumor, and the complete absence of pulmonary symptoms suggests that such was not the case. Having eliminated these two possibilities we are left with the diagnosis of a mediastinal tumor, apparently arising in the posterior mediastinum and extending into the right side of the chest.

The next question is whether it was benign or malignant. Dr Holmes has mentioned that the general homogeneous smooth appearance suggests a benign lesion. One must pay close attention, however, to the clinical story, and in the same connection consider the question how long the lesion had been present. It seems likely that it had been there for more than nine months. The absence of respiratory symptoms suggests that it was a rather slowly growing process and one would like to suppose, therefore, that it had developed over an even longer period of time. In this connection the question of a congenital cyst might be raised, and although the patient was sixty-five years old, such a lesion is still a possibility. Then again we have some indication to suggest that there was a definite lesion in the chest nine months before admission, because at that time the patient was sent to a thoracic surgeon. It is interesting that the clubbing was first noticed nine months before admission, but presumably it had been developing for a longer period of time. Does this mean that the lesion in the chest began at that time, or that there was some change in a previously

existing lesion that had not caused clubbing but because of the change began to do so? I really do not know. The systemic symptoms began at the time the clubbing was first noted, nine months before admission, when he first noted weakness, malaise, anorexia and weight loss. This suggests either a malignant tumor or a low-grade infection, possibly associated with necrosis and hemorrhage inside a previously existing mass. When the patient came to the hospital he had a low-grade fever, a slightly elevated white-cell count and an anemia, which are consistent with either a malignant tumor or low-grade infection.

The small lesion in the chest is interesting and possibly important. It suggests metastatic disease. An intravenous pyelogram was negative, and although the urine showed an occasional red cell, I believe that the negative x-ray films rule out a renal-cell tumor giving rise to lung metastases. The normal acid phosphatase test is against a prostatic carcinoma with metastases to bone, which might also give metastases to the lung. Also there is no x-ray evidence of bone involvement. There is a possibility that the small lesion came from the larger one. There is no evidence of any other primary disease in the body that could have been the source of the smaller tumor. As Dr Holmes said, it is unlikely that the large lesion is metastatic.

The laboratory data are of no help. All the findings are normal except for the chloride, which was slightly low for no obvious reason, and the prothrombin time, which was definitely abnormal. There is no mention of jaundice, and nothing to suggest that this patient had liver disease. I imagine that the patient received vitamin K before operation. I wonder whether the prothrombin time was redetermined and whether there was any change.

DR BENJAMIN CASTLEMAN The test was repeated, and there was no change.

DR LINENTHAL Finally, the real problem in this case is the diagnosis of the pulmonary tumor. I do not believe that I am going to be able to make a definite diagnosis. All I am able to do is mention a few of the possibilities.

The lesion said to be most frequent in the posterior mediastinum is a tumor of neurogenic origin, a neurofibroma, which may go on to cystic degeneration and hemorrhage. I can see no way of being sure of such a tumor. This, I believe, may become malignant, but there is nothing in the x-ray appearance of the tumor to suggest that.

The possibility of lymphoma must also be mentioned, but the lesion is too smooth in outline and there is no way of being sure of that diagnosis unless one knew how it responded to x-ray therapy. A congenital cyst can occur at this age. I believe, however, that there is often x-ray evidence of attachment to or encroachment on the trachea or esophagus. There is nothing here to help in that respect. Another possibility is a tumor arising in other tis-

sues, such as a lipoma. Then, there is dermoid cyst, but I know no way of making this diagnosis unless one finds changes of density by x-ray or unless rupture into a bronchus leads to the raising of characteristic material. Furthermore, the patient is too old for such a tumor.

Echinococcal cyst was thought about, but the skin test was negative. It is, I think, positive in a high percentage of these cases.

I suppose one should always mention tuberculosis. It is interesting that on physical examination there was an area of dullness at the left apex, but the x-ray appearance of that region was apparently normal, so that I cannot see how one can go any farther.

I see no easy way of choosing between these possibilities. The best I can do is to put, as my first diagnosis, a tumor of the mediastinum, possibly cystic, with malignant degeneration, associated with hypertrophic pulmonary osteoarthropathy.

DR RICHARD H. SWEET: On the surgical service we have been impressed by the fact that extensive pulmonary osteoarthropathy seems to be associated more frequently with tumors of the lung and mediastinum, usually malignant ones, than with infections. Certainly I think that it would help you to exclude tuberculosis, benign cyst and dermoid cyst. I do not recall having seen osteoarthropathy with either of these conditions. The most extensive pulmonary osteoarthropathy that we have encountered has been in cases of carcinoma of the lung.

DR CASTLEMAN: Dr Herrera, will you tell us what you found at operation?

DR RODOLFO E. HERRERA: At the time of operation the small tumor in the upper chest wall proved to be a lipoma. The large tumor filled the entire right lower lobe. It had not extended to the chest wall, and so far as could be ascertained there were no enlarged lymph nodes in the mediastinum or in the hilus. The fissure between the middle and lower lobes was almost nonexistent, whereas it was almost complete between the middle and upper lobes. It was therefore much easier to remove the middle lobe with the lower lobe than to do a lower-lobe lobectomy, and this was done. The procedure also allowed the resection to be carried out far away from the tumor, which we believed grossly was a fibrosarcoma.

DR SWEET: I advised Dr Herrera to determine first the nature of the tumor in the chest. If it were a metastasis from the large tumor, pneumonectomy would have been unwise.

CLINICAL DIAGNOSES

Metastatic tumor of lung
Hypertrophic osteoarthropathy

DR LINTHALL'S DIAGNOSES

Malignant mediastinal tumor
Pulmonary hypertrophic osteoarthropathy

ANATOMICAL DIAGNOSES

Fibrosarcoma of lung
(Hypertrophic osteoarthropathy.)

PATHOLOGICAL DISCUSSION

DR CASTLEMAN: The specimen that we received was a large, round, well encapsulated tumor filling almost the entire right lower lobe (Fig 2). In places



FIGURE 2 Photograph of a Cross Section of the Resected Tumor in the Right Lower Lobe

it was necrotic. This turned out to be a fibrosarcoma. Whether this was a primary sarcoma of the lung or perhaps metastatic could not be determined grossly. I do not believe, however, that I have ever seen a metastatic tumor that had reached this size.

Do you want to tell us what happened after operation, Dr Herrera?

DR HERRERA: The patient had an uneventful postoperative course and was discharged at the end of the second week. From the first day after operation he was completely relieved of his joint symptoms. He volunteered the information that the stiffness and pain were completely relieved and remained so until about two months later, at which time his complaints were no longer centered in the extremities but along the spine and in the left lower quadrant of the abdomen. When x-ray films of the spine were taken, it was apparent that he had wide-

spread metastatic involvement of the vertebrae. There was a small nodule at the tumor end of the thoracotomy wound, which on removal showed recurrence of the fibrosarcoma. He went downhill rapidly and died of bronchopneumonia within three or four weeks.

DR HOLMES: The films that were taken later of the hands and wrist show much less evidence of periosteal reaction, apparently they improved. The appearance in the spine is not too conclusive, there is a mottled appearance, but before committing myself on that I should like to be sure that it was a constant finding.

DR SWEET: I have had one exception to Dr Castleman's statement that a single large tumor like this cannot be metastasis. In a patient whom I saw six or seven years ago there was a single metastasis this size in the right lung from a previously resected sarcoma of the breast. I wonder if sarcoma may not be an exception to that statement.

DR CASTLEMAN: I do not doubt that a metastasis can reach this size, but I do not believe that I have ever seen one.

Unfortunately we were unable to get permission for an autopsy and do not know whether the lesions in the spine were metastatic.

DR HOLMES: You still do not know whether the one in the lung was metastatic?

DR CASTLEMAN: Clinically he had no evidence of a primary tumor elsewhere.

DR MARIAN W. ROPES: The rapidity of the disappearance of bone and joint symptoms is extremely interesting. It came within a few hours after the operation. It is interesting to determine how soon the bone changes disappeared. These films were taken two months after operation and show considerable regression of the osteoarthropathy.

DR HOLMES: Do the periosteal changes completely disappear?

DR ROPES: According to the literature that has occurred. We have never had an opportunity to follow them completely enough to see. It is unfortunate that we did not have the chance to see the histologic appearance of the bones in this case.

I agree with Dr Sweet that the severest pulmonary osteoarthropathy that we have seen has been in cases of malignant disease rather than in cases of infection.

CASE 31272

PRESENTATION OF CASE

A seventy-four-year-old man was admitted to the hospital because of abdominal distress and hematemesis.

The patient was well until a week before admission, when he began to notice abdominal fullness

after eating. Flatulence gradually increased, and he became moderately anorexic and experienced periodic nausea. He had a normal bowel movement on the day before admission. On the day of entry he felt more distress than usual. He drank a "rum coke," then went to see his physician. En route to the physician's office he became acutely nauseated and vomited once. While in the office he repeatedly vomited dark fluid containing blood and had an episode of severe agonizing pain radiating from the epigastrium through the lower abdomen to the back and legs. While vomiting he fainted, fell and struck his head on the floor, bruising the left side of the face. He was taken promptly to this hospital.

He had had malaria fifty-three years before entry. He had had pneumonia on two occasions, once fifty-two years before entry and once nineteen years before entry. Six years before admission he had an appendectomy, with drainage, for a perforated appendix. Complicating abdominal-wall and scrotal abscesses were incised and drained. The post-operative period was also thought to have been complicated by a transient toxic hepatitis. He was discharged well five weeks after admission. Three and a half years before admission the patient had had a cholecystostomy for empyema of the gall bladder. At that time a blood Hinton test was positive but a Wassermann test was negative. After three weeks in the hospital he was discharged with a small draining sinus. This ceased to drain a few weeks later, and he remained well until the present illness.

Physical examination revealed a thin man with extremely pale skin and mucous membranes. There were massive periorbital and subconjunctival hematomas on the left side. The abdominal scars were well healed, a moderately sized defect of the abdominal wall was noted below the paramedian incision. Vision was poor. The eyes reacted to light and distance. The heart and lungs were normal. Abdominal examination was essentially negative. There was no tenderness or spasm. No organs or masses were felt. Peristalsis was normal. Rectal examination revealed a normal prostate and no masses or tenderness. A glove specimen of feces was soft and dark and gave a + + + + guaiac test.

The temperature was normal, the pulse 80, and the respirations 20. The blood pressure was 160 systolic, 80 diastolic.

Examination of the blood showed a white-cell count of 18,300. The urine gave a + test for albumin and a green reaction with Benedict's solution, the sediment contained 25 white cells, 2 to 3 red cells and many hyaline and granular casts per high-power field. The serum nonprotein nitrogen was 36 mg per 100 cc, and the protein 5.6 gm. The chloride and bilirubin were normal. The prothrombin time was 24 seconds (normal, 18 to 20 seconds).

An x-ray examination of the skull showed a fracture of the base of the left zygoma and a fracture of the root of the left maxillary antrum, with depression and clouding of the antrum. There was a questionable fracture of the roof of the left orbit, without additional deformity. In the right occipital area there was an indistinct line of decreased density running in a longitudinal direction for about 9 cm. A barium enema was negative. X-ray examination of the chest was negative, and no free gas was seen below the diaphragm. A gastrointestinal series showed a normal stomach and esophagus by fluoroscopy. The duodenal cap was slightly irregular, and no crater was seen with the fluoroscope. On the film, the duodenal cap showed an area in which the barium pooled, suggesting a crater. A plain film of the abdomen on the next day showed a large amount of barium remaining in the dilated stomach. This dilatation was not present at the time of the gastrointestinal examination on the previous day. There was a small amount of barium in the small bowel, and the colon was fairly well outlined.

At 3:00 a.m. on the third hospital day the patient became apprehensive. The skin was cold and clammy. He complained of severe pain in the abdomen, but this was negative on examination. An hour later he vomited forcefully a large amount of reddish-brown, foul-smelling fluid and the blood pressure was 130 systolic, 75 diastolic. He continued to vomit and passed a soft reddish-brown stool. The vomitus and the stool showed ++++ guaiac tests. At 6:00 a.m. he went into shock, becoming momentarily pulseless and very dyspneic. He vomited again and promptly appeared considerably better, with a strong pulse of 70 and a blood pressure of 130 systolic, 60 diastolic.

At 6:00 p.m. on the fourth day he appeared somewhat improved, with normal temperature, pulse and respirations. About two and a half hours later he was found to have expired. He had passed a moderate-sized, dark-red, tarry stool.

DIFFERENTIAL DIAGNOSIS

DR. GEORGE MARKS: There is evidence of a variety of lesions in this history. Through it all runs the theme of normal temperature, pulse and respirations, up to practically the last gasp. The question is, Which of the many lesions accounted for his sudden death? The past history contained numerous fairly major episodes: malaria, a drained appendix, cholecystostomy and a positive Hinton test. Yet it says in the beginning that he had been well until a week before admission. Apparently there was no particular loss of well being, at least from the last previous episode to his present entry. He obviously was sick when he arrived, in spite of the temperature, pulse and blood pressure, which presumably was not that of shock, although of course he may have been running a considerably higher pressure before

he arrived in the hospital. At entry the pressure was 160 systolic, 80 diastolic.

The first point that seems to carry a good deal of significance is the initial attack in the doctor's office, following a week of gradually increasing abdominal distress. Apparently in the beginning it was not an actual pain as much as a feeling of fullness and discomfort. It was somewhat periodical, and the patient had occasional nausea. He had an acute incident, in that he fainted, fell on his face and head and suffered fractures. I assume from the record that he was not unconscious when he arrived in the hospital, although that is not brought out specifically. The blood pressure and pulse do not indicate any change in intracranial pressure. So I am going to disregard the acute accident among other things, considering that it had no particular bearing on his death.

He was promptly x-rayed. The stomach was found to be negative, but there was a suggestive lesion in the duodenum at the first examination and at a subsequent one. I presume the second one was a twenty-four-hour plate. I have been told by the x-ray experts that films are of much less value than fluoroscopy, but I should like to see the films.

DR. MILFORD D. SCHULZ: I think that this is probably what was interpreted as a duodenal ulcer. There are no spot films, since we have to depend on the fluoroscopic observation in this day of film shortage. Only a single film of the stomach was made. Certainly there is a marked change in the appearance of the stomach in the film taken the following day. The stomach is greatly dilated, and there is a large amount of residual fluid and barium within it.

DR. MARKS: The question resolves itself into whether this man could have run the course that he did from hemorrhage from such a lesion as a duodenal ulcer. On examination he is described as having a negative abdomen, which he might have had if it were only a small hemorrhage. A large amount of blood in the intestinal tract will produce tenderness and generalized discomfort on palpation, but he apparently did not have those signs. He was not distended. During the course of the first three or four days in the hospital he developed gastric distention and pain, which was relieved by vomiting, this fits in with the distention that caused a disturbance of his intestinal tract from the duodenum on down.

Going back again to his initial attack of pain, the one that was so agonizing that he fainted and fell, I think the possibility of pancreatitis has to be considered. On the other hand, if pancreatitis were present and produced that much pain I should expect that something would have been found on physical examination. Apparently the abdominal examination did not bear out a fulminating pancreatitis.

Did he have a pin-point perforation of an ulcer, with a little fluid escaping now and then? That is possible, and between the escape of fluid he could have had a relatively negative abdomen. Yet, a pin-point ulceration of that sort, even when perforated, does not lead to sudden death.

Shall we pay any attention to the gall-bladder history? There is one point in the laboratory findings, the slightly lengthened prothrombin time, that perhaps represents some disturbance of liver function. Since it was not marked, since the blood bilirubin was not high and since the patient apparently was not jaundiced, it may have been secondary to his general condition. The urinary findings, to my inexperienced eye, could represent his seventy-four years, with nephrosclerosis.

There is perhaps one thing that covers his major disorder as well as any, namely, a dissecting abdominal aneurysm. Its first appearance was perhaps before the attack in the doctor's office, which represented the beginning of dissection, later there was disturbance of the innervation of the intestinal tract, and possibly the circulation. I should expect, however, that he would have had more local abdominal signs if he had had a circulatory disturbance of the intestine. I have to consider mesenteric thrombosis, although mesenteric thrombosis certainly has local signs.

I visualize this sequence of events as a dissecting aneurysm that at first progressed slowly and then involved the duodenum, the portion of the intestinal tract that overlies the aorta retroperitoneally, with eventual rupture causing sudden death. There is nothing in the physical examination referring to nerve or circulatory changes in the lower extremities, the blood pressure readings and so forth?

DR BENJAMIN CASTLEMAN: None were observed.

DR MARKS: It seems to me that this case is one of death from hemorrhage, and to my way of thinking we have not enough evidence of sudden intra-intestinal or intragastric hemorrhage to explain the picture on that basis.

Sudden hemorrhage may occur from gastritis. Whether the taking of a "rum coke" on the way to the doctor's office was a habit or just to bolster up his morale we do not know. Acute gastritis following bouts of alcoholism can produce massive bleeding. My impression from the history is that there was not a great amount of actual blood, although blood was constantly found in the contents of the stomach and large intestine. I shall rest the case by saying that this was a dissecting aneurysm with final rupture. He had had one positive Hinton test, but whether or not the aneurysm was syphilitic in origin I shall not attempt to say. The x-ray picture may represent ulcer, although I am inclined to believe that the spasm noted by x-ray in the duodenum was secondary to the retroperitoneal lesion.

CLINICAL DIAGNOSIS

Carcinoma of stomach?
Coronary thrombosis?

DR MARK'S DIAGNOSIS

Dissecting aortic aneurysm, with rupture

ANATOMICAL DIAGNOSES

Duodenal ulcers, bleeding
Acute and chronic gastritis
Hemorrhage into the gastrointestinal tract

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy this patient's stomach was filled with about 700 cc of fresh clotted blood and the entire gastrointestinal tract was also filled with blood. There were probably two sources for the hemorrhage. He had two duodenal ulcers just beyond the pylorus, one of which was an obvious source of the bleeding, the other source may have been the severe gastritis, which involved almost the entire mucosa. The mucosa was markedly injected, raised and pebbly. I believe that most of the bleeding, however, originated from the duodenal ulcer. That was the complete story.

DR MARKS: How do you explain the pain in the back and down the middle of the leg?

DR CASTLEMAN: Dr Jones has described pain in the back in the duodenal ulcer. I cannot explain the leg pain.

DR MARKS: Was the ulcer on the posterior wall of the duodenum?

DR CASTLEMAN: Yes. Those are the ones that frequently bleed.

DR JONES: Was there a large vessel in the middle of a fairly large ulcer?

DR CASTLEMAN: The ulcer was not large, it measured 1 cm in diameter and did have a protruding eroded vessel in its center. Apparently the patient must have bled before admission, the bleeding stopped when he came into the Emergency Ward but began again on the following day.

DR MARKS: Was it an acute ulcer?

DR CASTLEMAN: It was an acute erosion of an old ulcer. There was definite evidence of old ulceration.

DR JONES: There is one thing that may be of some importance. As Dr Marks pointed out, this patient was seventy-four years old and the story these people tell is frequently different from that of a younger person. It is not uncommon to have bleeding from an ulcer without pain at the time of hemorrhage, but it is not too common to have chronic ulcer and no symptoms whatever. Those in the older age group, however, often have no symptoms and may even perforate without pain. They do not perceive pain as readily as a younger person, and that may change the story a bit.

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HIGH LIGHTS OF THE MEETING OF THE EXECUTIVE COMMITTEE OF THE COUNCIL

ONE could not have participated in the recent meetings of the Council of the Massachusetts Medical Society without having been impressed with how widespread the Society's activities have become. The vision created by such activities takes this organization out of its semicloistered past and places it squarely in the middle of an active and turbulent world.

The time consumed by the Council in the consideration of these necessary activities has caused many to believe that some change in its method of

procedure is called for. Certain steps in this direction have already been taken. The publication of the agenda in advance of the Council meeting is one of them. The formation of the Committee on Council Rules and the subsequent adoption of certain rules of procedure comprise another. It is quite likely that additional rules need adoption, — for example, limitation of the time of debate, — if the conduct of the business of the Society is to keep pace with the fast moving tempo of the times. Rules, however, that are not enforced and in whose enforcement the Council shows no interest will never solve the problem. Such rules are of importance only if they reflect the willingness of the Council to exercise this kind of self-discipline.

The annual meeting of the Council was not held this year because of the restrictions imposed by the ODT. In lieu of this meeting the Executive Committee of the Council met on May 23, 1945. The meeting was called to order at 10:30 a.m. and continued in session, except for a short recess for luncheon, until after 5:00 p.m.

The report of the Treasurer showed the excellent state of the Society's finances.

The report of the Subcommittee on Labor and Industry of the Committee on Public Relations spoke of the committee's conferences with labor and industry and of what it had learned of their respective points of view regarding the distribution of medical care. It emphasized the opportunities that such conferences give to publicize the Society's attempt along these lines through the aegis of the Blue Shield.

The Subcommittee on Public Information of the Committee on Public Relations strained hard at the traditional moorings of the Massachusetts Medical Society. Its report favored the Society's use of paid newspaper and magazine advertising as a means of getting over its messages to the public. That there has been considerable change in the thinking of the Council along these lines is evidenced by the fact that the subcommittee was directed to continue its study and by the further fact that a thousand dollars was placed at its disposal for the purposes of the study.

The supervision of the Medical Information Bureau was turned over to the Subcommittee on

Postgraduate Education of the Postwar Planning Committee

The report of the Committee on Legislation demonstrated that this committee has made full use of the Society's potentialities. The action of the Legislature on June 6, 1945, in referring to the next General Court a bill that would specifically exempt, until July, 1949, a substandard school from the provisions of the Medical Practice Act seems to bear this out. In this connection, however, it must be remembered that the so-called "Chiropractic Bill" is still before the Legislature. The Society owes much to the vigorous leadership of this committee.

The report of the Committee on Society Headquarters recognized the inadequacy of the space now allotted to the administrative activities of the Society. It offered certain solutions, and was authorized to pursue this subject along the lines recommended.

The Postwar Loan Fund was finally authorized, and an initial sum of \$25,000 from the Society's funds was set aside for this purpose. The administrative details have been placed in the hands of a new committee, which has already been appointed by the President.

The report of the Committee on Medical Education showed commendable activity. Under the G. I. Bill of Rights the veteran is entitled to certain opportunities to further his education. Regarding the educational opportunities that relate to the healing arts, there is grave danger that the veteran may spend his time and effort in a school that cannot adequately prepare him in the chosen field. The committee has offered advice in this regard to the Massachusetts Department of Education. The advice was gladly received, and assurance was given of its continued use. This department certifies to the Veterans Bureau the schools that are suitable for training under the bill.

Although the Committee on Rehabilitation offered no report, certain information came to the Executive Committee concerning its activities. The Massachusetts Department of Rehabilitation, as part of its program, is taking notice of those who are in what is termed "a state of static remediable disability." Briefly, this refers to the person

who, because of a disability that is static and remedial, cannot take his rightful place in the community. The department proposes to pay the expenses, both hospital and medical, of his rehabilitation. The person's inability to meet the expense involved must be shown, but indigence need not be proved. The Committee on Rehabilitation is at present working with the department on a fee schedule that will cover physicians' services under this heading.

The revival of the New England Medical Council, defunct since 1933, was the subject of a communication from the Rhode Island State Medical Society. The Executive Committee voted to participate.

The President spoke of a meeting that he had recently attended in Michigan. He said that the presidents of seventeen other state medical societies were present. He referred to a resolution that had been adopted at this meeting, part of which called for the creation of a planning committee in each of the states represented and in such other states as wished to participate. It would be the function of these committees to study problems of national interest. They severally would meet from time to time for exchange of views. In the thought behind this movement there was no intention to interfere in any way with the functions or prerogatives of the House of Delegates of the American Medical Association. It was hoped that this type of organization might be of help to the Council on Medical Service and Public Relations of the American Medical Association. The Executive Committee voted to participate in this matter and designated the Committee on Public Relations as the agency of the Society best suited to this purpose.

SECOND ANNUAL REPORT OF THE CHILDREN'S CENTER

A YEAR and a half ago, the *Journal* commented editorially on the most recent addition to Boston's community of medical institutions, the Children's Center in Roxbury, and reviewed briefly its activities and its accomplishments from its establishment in January, 1943.*

The Center has now published its second annual

*Editorial: The Children's Center. *New Eng. J. Med.* 229:732, 1943.

report, a sign that it has passed through its uncertain years of infancy and has emerged into its increasingly fruitful, if still somewhat youthful, period of maturing development. Interested friends and well-wishers can now view its aims and purposes with a better perspective, and no doubt its directors and staff will admit that they, too, can see more clearly the road that they are traveling.

The purpose of the Children's Center is an extremely fundamental one — to go back so far as possible toward the beginning of human behavior patterns, to attempt to analyze the cause of failure in adjustment and to set up machinery by which it can be corrected. According to the introductory words of the report, "the second year of the Children's Center has brought gratifying progress toward its goal as an institute where emotionally disturbed young children may be helped to lead happy and useful lives, and where a fuller understanding may be gained of the factors which make for harmony or disharmony in the development of the human personality."

That referring agencies and the community at large have come to an appreciation of the purposes of the institution is attested by the fact that, although fewer applications for enrollment have been made, the percentage of acceptances, owing to their suitability, has greatly increased.

An important and unique factor in the success of this organization is its employment of the nursery school as a means of studying and retraining the child, thus providing re-education of the emotionally disturbed subject in a group setting. Individual psychotherapy is started at the same time, and conferences with the parent complete the triad of therapeutic measures.

An institution such as this, if it is to achieve its highest degree of usefulness, must, in addition to therapy and research, assume the obligation of teaching. This the Children's Center has done by providing, during the past academic year, field work for two social workers, two students of psychiatric social work, eight nursery-school students and a psychiatric fellow assigned to the Judge Baker Guidance Center. Furthermore, nurses in training at the Boston City Hospital have come two at a time to assist in the nursery school, and members

of the staff have been utilized for lectures and seminars given to various groups in the community.

All in all, the Children's Center appears to be successfully and eminently fulfilling the aims that have been conceived by its sponsors, directors and staff.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

McPHERSON — George E. McPherson, M.D., of Amherst, died June 16. He was in his sixty-ninth year.

Dr. McPherson received his degree from Baltimore Medical College in 1904, and became a staff member at the Carney Hospital, South Boston, in 1912. He left there to become neuropsychiatric specialist at the Sturdy Memorial Hospital in Attleboro and later became superintendent at the Foxboro State Hospital. He served for two years as assistant executive officer at the Boston Psychopathic Hospital and assistant superintendent at the Medfield State Hospital. He was superintendent at the Belchertown State School for twenty-one years before his retirement. He was a fellow of the American Medical Association.

His widow, a daughter, a son and five grandchildren survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR MAY, 1945

DISEASES	RÉSUMÉ		
	MAY 1945	MAY 1944	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	1	1	1
Chancroid	1	3	*
Chicken pox	1122	2,60	1207
Diphtheria	14	21	11
Dog bite	1321	1388	1335
Dysentery bacillary	19	34	12
German measles	167	381	382
Gonorrhea	484	440	358
Granuloma inguinale	2	0	*
Lymphogranuloma venereum	3	4	*
Malaria	146	68	0
Measles	996	4208	4209
Meningitis meningococcal	19	42	8
Meningitis Pfeiffer-bacillus	0	2	2
Meningitis pneumococcal	5	6	5†
Meningitis staphylococcal	0	0	0†
Meningitis streptococcal	1	2	0†
Meningitis other forms	4	1	1†
Meningitis undetermined	1	16	10†
Mumps	2222	1459	977
Pneumonia lobar	261	291	291
Salmonella infections	3	16	16
Scarlet fever	1521	1500	1120
Syphilis	388	439	507
Tuberculosis pulmonary	519	220	279
Tuberculosis other forms	19	13	23
Typhoid fever	0	2	2
Undulant fever	2	7	4
Whooping cough	673	724	635

*Made reportable December 1943.

†Four year average.

COMMENT

Diphtheria recorded a welcome reduction of 10 cases from the previous month. Incidence is now only moderately high as compared to the seven-year median.

Meningococcal meningitis showed a slight lowering of its previous high level relative to the seven-year median. Case incidence for the month of May of last year was more than twice that for the present May and that for May, 1943, four times the present figure.

Mumps maintained its seasonal downward trend.

This is the first time that not a case of typhoid fever was reported in the month of May.

Pulmonary tuberculosis showed an increase and was moderately above the seven-year median. In part, this reflected the results of intensified case-finding programs, which will influence the figures for some time. The great increase in tuberculosis predicted as a result of the war has not materialized.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Camp Myles Standish, 1, total, 1.

Diphtheria was reported from Arlington, 1, Boston, 5, Camp Edwards, 1, Camp Myles Standish, 1, Chelmsford, 1, Framingham, 1, Lawrence, 1, Melrose, 1, New Bedford, 1, Salem, 1, total, 14.

Dysentery, bacillary, was reported from Boston, 1, Holyoke, 1, Springfield, 1, Worcester (State Hospital), 16, total 19.

Encephalitis, infectious, was reported from Yarmouth, 1, total 1.

Malaria was reported from Boston, 1, Camp Edwards, 81, Cushing General Hospital, 3, Fort Devens, 44, Northampton (U S Veterans Hospital), 5, Waltham Regional Hospital, 11, Worcester, 1, total 146.

Meningitis, meningococcal was reported from Boston, 5, Brookline, 1, Cambridge, 1, Dartmouth, 1, Everett, 1, Haverhill, 1, Lowell, 1, Lynn, 1, New Bedford, 1, North Attleboro, 1, Quincy, 1, Seekonk, 1, Somerville, 1, Springfield, 1, West Bridgewater, 1, total, 19.

Meningitis, pneumococcal, was reported from Andover, 1, Boston, 1, Cambridge, 2, Northampton, 1, total, 5.

Meningitis, streptococcal, was reported from Arlington, 1, total, 1.

Meningitis, other forms, was reported from Boston, 1, Cambridge, 1, Norwood, 1, Worcester, 1, total 4.

Meningitis, undetermined, was reported from Worcester, 1, total, 1.

Salmonella infections were reported from Boston, 2, Newton, 1, total, 3.

Septic sore throat was reported from Boston, 2, Fort Devens, 1, Merrimac, 2, Somerville, 2, Williamstown, 2, Worcester, 1, total 10.

Trichinosis was reported from Boston, 1, Somerville, 1, Worcester, 1, total 3.

Undulant fever was reported from Paxton, 1, Pembroke, 1, total 2.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Salem	July 2	Paul W. Hugenberger
Lowell	July 6	Albert H. Brewster
Haverhill	July 11	William T. Green
Brockton	July 12	George W. Van Gorder
Pittsfield	July 16	Frank A. Slowick
Springfield	July 17	Garry deN. Hough, Jr.
Worcester	July 20	John W. O'Meara
Fall River	July 23	Eugene A. McCarthy
Hyannis	July 24	Paul L. Norton

MISCELLANY

SOCIAL AND ENVIRONMENTAL FACTORS IN MEDICINE

The teaching of the social and environmental factors in medicine, as now carried on in medical schools in this country, is being studied by the Association of American Medical Colleges in co-operation with the American Association of Medical Social Workers. A grant to finance the study has been given by the Milbank Memorial Fund. A committee of twenty-five physicians and medical social workers who are engaged in this teaching has been formed to direct the study, under the name of the Joint Committee on the Teaching of the Social and Environmental Factors in Medicine. The co-chairmen are Dr. J. A. Curran, president of the Long Island

College of Medicine, and Miss Eleano. Cockerill, associate professor of social case work at the School of Applied Social Sciences, University of Pittsburgh. A centrally located project subcommittee has been set up under the chairmanship of Dr. J. E. Rhoads, assistant professor of surgical research and acting director of the Harrison Department of Surgical Research, University of Pennsylvania School of Medicine. The executive secretary of the study is Miss Harriett M. Bartlett, 49 Fruit Street, Boston 14.

It is the aim of the study to bring together and analyze the experience of a group of medical schools in introducing students to the social and environmental components in medicine. Visits to selected centers will be made by members of the committee. The study is expected to last through 1947, at the end of which time a report summarizing the findings will be prepared.

NOTE

The official corporate name of the Newton Hospital has been changed to the Newton-Wellesley Hospital, the necessary action having been taken by the members of the Corporation and approval thereof secured from the Commissioner of Corporations and Taxation.

BOOK REVIEW

Strophanthin. Clinical and experimental experiences of the past twenty-five years. By Bruno Kisch, M.D. 8°, cloth, 158 pp., with 24 illustrations. New York: Brooklyn Medical Press, 1944, \$4.00.

Kisch has done a useful service in summarizing the present status of the use of strophanthin and the history of its introduction in the therapy of heart failure. The small volume is well printed but is expensive.

There are seven chapters and a bibliography of thirty pages. In the preface, the author leaves out, in the opinion of the reviewer, the most important reason why Americans have not adopted strophanthin more generally and routinely, that reason being the excellent experience they have had with the intravenous use of digitalis preparations, which has so sufficed in emergency treatment that strophanthin has been simply an alternative. Kisch speaks of the experience in the United States as being characteristic of that throughout the Western Hemisphere, but in Latin America strophanthin has been in regular use.

The historical introduction is extremely interesting and is worth while reading in toto. The clinical applications of the drug are clearly presented in Chapter 5.

This book can be recommended to all those interested in the treatment of heart disease.

NOTICES

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JULY 12

FRIDAY, JULY 13

*9:00-10:00 a.m. Medical clinic. Isolation Amphitheater. Children's Hospital.

10:30 a.m. Introduction to Dermatology. Dr. John G. Downing (Postgraduate clinic in dermatology and syphilology). Amphitheater. Mallory Building. Boston City Hospital.

12:00 m-1:00 p.m. Clinicopathological conference (Boston Floating Hospital). Joseph H. Pratt. Diagnostic Hospital.

MONDAY, JULY 16

*12:00 m-1:00 p.m. Clinicopathological conference. Peter Best. Brigham Hospital.

TUESDAY, JULY 17

*9:00-10:00 a.m. Medical clinic. Infants Hospital.

*12:15-1:15 p.m. Clinicoradiological conference. Peter Best. Brigham Hospital.

WEDNESDAY, JULY 18

*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

SEPTEMBER 17. American Public Health Association. Page 752. 1946.

OCTOBER 1-6. Mediocolegal Conference and Seminar. Page 776. 1946.

of June 28.

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THE HISTORY OF MIDDLESEX NORTH DISTRICT MEDICAL SOCIETY 1844-1944*

ARCHIBALD R. GARDNER, M.D.

LOWELL, MASSACHUSETTS

CONDENSATION of time and space is one of the important characteristics of this civilization, and, as this is the centennial anniversary of our local society, an attempt will be made to condense one hundred years of its growth within the short time allotted. The great historian Livy complained of the scant records of the early history of Rome, but that was not my difficulty in this case. My problem was to select from the abundance of records some topics that might be of interest to you. Most of us like people better than dates, which is indeed an essential trait of physicians. There are, however, a few dates and associations of our early society's chronicles that will give a historical perspective.

No discourse pertaining to the history of the Middlesex North District Medical Society should be given without a clear statement of its relation to its parent, the Massachusetts Medical Society. The latter, founded one hundred and sixty-three years ago, is the oldest medical society in the United States with a record of uninterrupted activities from its founding to the present time.

In the Charter Act of the Legislature of 1781, there was no provision for the forming of local or district medical societies, integral parts of the parent society, in the different sections of the Commonwealth. These district or county medical societies have since become prominent features of all state medical societies, their boundaries usually conforming to counties.

In 1829 the first medical association in Middlesex County was formed. The meeting was held in Lexington. Dr. Josiah Bartlett, of Chelmsford, was chosen president, and Dr. F. S. Hurd secretary. The physicians of Lowell who were present at that meeting were Drs. Green, Huntington, Crosby and Bartlett. Unfortunately, the records of this association have been lost.

In 1833 the members were forced to dissolve their association on account of the time and expense involved in going by stage to and from their then distant places of meeting, and for several years there

was no formal organization or association of physicians in this vicinity.

The town of Lowell was rapidly growing, following the building of its fine system of canals, which so greatly contributed to the ever increasing textile industry. By 1836 the town had become a city. Keeping pace with this growth, the number of physicians was increasing, and the old association had awakened a spirit, for in man there is an instinct to band with others for mutual benefit, not alone in matters of government, but also for the help derived from aggregate knowledge and experience, this being especially true regarding the followers of our calling. So it was but natural that another medical association should be formed.

In 1839, a special meeting of Lowell physicians was held at the office of Dr. J. D. Pillsbury to organize a society for mutual improvement, at which time the Lowell Medical Association was formed. The following physicians were present: Elisha Bartlett, John C. Dalton, James W. Ford, J. W. Graves, William Grey, J. P. Jewett, Gilman Kimball, George Mansfield, Daniel Mowe, Hiram Parker, Otis Perham, Harlin Pillsbury, J. D. Pillsbury, J. W. Scribner, Benjamin Skelton and Daniel Wells. This voluntary association of high character continued to grow in numbers and increase in interest until at the end of five years a request was made by some members of the Massachusetts Medical Society, resident in this vicinity, for the establishment of a district medical society.

The committee reported at the October meeting in that year that they had drawn up a petition for such a society, which had been signed by twenty-three out of twenty-seven fellows residing in the proposed district, and accordingly recommended that a charter be granted. This was passed promptly by a unanimous vote. The petition follows:

The undersigned members of the Massachusetts Medical Society, resident in the northerly section of the County of Middlesex, believe that the establishment of a district medical society within its limits embracing the following towns, namely: Lowell, Billerica, Ashby, Townsend, Pepperell, Dunstable, Groton, Shirley, Tyngsboro, Chelmsford, Carlisle, Littleton, Dracut, Tewksbury, Concord, and Acton (the meetings of which shall be holden in the City

*An address delivered at the Centennial Observance of the Middlesex North District Society, December 6, 1944.

of Lowell) would be of great utility. Being desirous of enjoying the advantages and privileges of such an institution, we do hereby pledge ourselves (should a petition for a charter to that effect already in the hands of the Councillors be granted) to become active members of the same, by attending its meetings and otherwise promoting the interest as opportunity may occur.

This charter was received November 2, 1844, and the society was known as the Middlesex District Medical Society.

In 1850 a slight change was made. Middlesex County was divided into three districts—east, north and south. This city and eighteen neighboring towns were included in the North District, and the name of the society was changed to the Middlesex North District Medical Society, which it has retained ever since. The caliber of the members in the society of that period can be judged from the fact that in their desire to perpetuate their knowledge of medical science Dr. Elisha Huntington petitioned the Legislature for a charter to establish a medical school in Lowell.

In the formation of medical societies at that time, the objects were to combine physicians and surgeons duly qualified to serve the public as such, to point out the education to be pursued by those who should be desirous of entering our profession, to examine persons who had pursued this course and to give licenses to such as should be found qualified to engage in practice.

The medical societies in those years were the only organizations that controlled the standards of medical practice. It was not until 1894 that Massachusetts joined the majority of the other states of the Union in adopting a medical practice act, thereby establishing the Board of Registration in Medicine. This act, indeed, proved most undesirable, since it allowed incompetent doctors to be registered in the Commonwealth, but after years of constant efforts on the part of the medical societies, the Legislature was lately induced to correct conditions by passing a satisfactory bill. One has only to read the various advertisements in the magazines and journals of those days to note the extent of quackery and charlatanism. It has been stated that with the promotion of the local district medical society, the public in this locality had its first effective protection from those unscrupulous and dishonest medical pretenders.

The meetings of the earlier associations were held at the various members' homes for social converse, literary improvement and the exchange of fraternal courtesies. We later learn that meetings of the Middlesex North District Medical Society were held for thirty years in the Natural History Rooms of the Mechanics Building in Dutton Street, where the Genoa Club is now located. The first meetings held were in the nature of clinics where patients were examined free by three or more selected members. This practice was soon discontinued, and case reports were discussed, often with autopsy findings. Later, scientific papers were presented by members

who were selected alphabetically. During the last twenty-five years the papers have usually been given by members of the profession from the large centers and teaching institutions.

It is interesting to note the subjects of some of the addresses given in those early days at the meetings. For instance, Dr. John C. Dalton spoke on "Certainty in Medicine." One wonders just how much closer we have approached to "certainty" since that time. Dr. Zadok Howe, a family physician of Billerica, spoke of "Fear in Connection with Medicine." Without doubt this was the first psychiatric address ever given in this county. Fortunately, perhaps, he did not have the Freudian advantages of the modern-day specialist. "Cholera" was the subject of an address given by Dr. J. O. Green at a time when the disease was prevalent in the county. He also included in his paper a report drawn up by him as a member of a delegation consisting of himself, Dr. Bartlett and Dr. Huntington. These men had been appointed to investigate and report the nature, remedies and preventives of cholera, and were sent to New York by the select men of Lowell, one of whom was Dr. Josiah Crosby. This is early evidence of the importance of our society in its constant attention to affairs concerning the general public health.

The reports of the earlier meetings show that they were not so harmonious as those we are accustomed to attend. In fact, if it had not been for our legal connection with the state society, the district association would have been abandoned, since the dissensions among members were often long and loud. The subject of the controversies was usually based on questions of ethics and methods of practice.

There were periods when the meetings were not well attended. In 1879, it was voted that the meetings be followed by a dinner and the attendance was greatly increased with an interest that has never since lessened. The oft-repeated expression, "The way to a man's heart is by his stomach," is the keynote to the revival of this society.

Some of the most heated and lively discussions occurred at times when the community was in the throes of epidemics of scarlet fever, diphtheria, typhoid fever, meningitis, smallpox and cholera. The mere naming of this list of diseases, which were most prevalent in epidemic form during the early period of this society, impresses on one the tremendous advances that have been made in medicine since that time.

In those days, as now, the physicians and surgeons gave generously of their time and skill to charity. Of course they had a fee table, and it may be interesting to note some of the charges.

For a visit within one mile	\$ 75
Each additional mile	25
Visit in night (night is understood as beginning at 10 p. m. and ending at sunrise)	1 00
Advice in ordinary office cases	25
Advice in ordinary office cases and medicine	50

Small dressings at office	50
Extracting tooth	50
Each additional tooth	25
Obstetrical case	5 00
Amputation of fingers and toes	1 00 each
Reducing fracture of large limbs	5 00

Obviously there was no inflation in those days

It was stated in an editorial of the *Boston Medical and Surgical Journal* in 1847 that Lowell in 1846 contained 28,841 inhabitants. In that year there were 690 deaths, "pulmonary consumption," as everywhere in New England, swept off the greatest number, and scarlet fever was the next active agent in destroying human life. In the field of surgery, on the other hand, in another two years the world will be celebrating the hundredth anniversary of the greatest boon to modern surgery, namely, ether. It was only two years after the founding of our society that, within twenty-five miles from here, at the Massachusetts General Hospital, occurred the first public demonstration of the anesthetic properties of ether.

With the banishing of pain in operative cases there was still the specter of infection remaining, as in erysipelas, pyemia, septicemia, and gangrene, from which no surgical patient was safe. The work of Pasteur demonstrated that organisms and bacteria, airborne and otherwise, were the source of wound infections, following which Lister attempted to prevent infection by antiseptic methods. It was later in the eighties that the modern aseptic technic was developed. All this time members of our society were at work here in Lowell, first at the Corporation Hospital, where Kimball did his original and pioneer work under antiseptic methods, and later at St. John's Hospital, where aseptic technics were introduced and developed by some of our keen and progressive members.

Our fellows were well aware of the newer discoveries by engineers and scientists in public-health matters. Several members were the instigators and organizers of the Massachusetts Public Health Association.

In the early days of our society, the practice of medicine was more of an art than a science. It was largely carried on in patients' homes or doctors' offices. The doctors early learned that the best work could be done in hospitals, of which we have three—the old Corporation Hospital, organized in 1839 and now known as St. Joseph's Hospital, St. John's Hospital, founded in 1865, and the Lowell General Hospital, founded thirty years later.

The latter part of the century had become an age of science. Such diseases as tuberculosis, diabetes, pernicious anemia and some cases of cancer were no longer necessarily mortal diseases.

Within a few months following the publishing of the original paper describing the discovery of x-rays, forty-nine years ago, an x-ray picture of a coin and hairpin was taken through a book with an apparatus set up at the Lowell High School by Cyrus W. Irish and Arthur Gage. This is an example of the

alertness of our members to the importance of new scientific discoveries and their possible clinical application.

In the lifetime of this district society there has been more advance and progress in medical science than in all the centuries that preceded. One wonders what science will offer in the future. I hope, however, that a hundred years from tonight the menu will not consist of a couple of capsules and an intravenous infusion administered by a white-garbed nurse to each as he enters the banquet hall.

As I stated earlier that we like people better than dates let us turn to some interesting and important personalities outstanding in the history of our society.

Among the men who led in conducting the affairs of the society in those early years are the following first officers elected: Dr. Nehemiah Cutter, of Pepperell, president, Dr. Elisha Huntington, of Lowell, vice-president, Dr. John D. Pillsbury, of Lowell, secretary, Dr. J. P. Jewett, of Lowell, treasurer, Dr. J. W. Scribner, of Lowell, librarian, and Drs. Augustus Pierce, of Tyngsboro, Elisha Huntington, of Lowell, and Harlin Pillsbury, of Lowell, members of the Standing Committee.

Dr. David N. Patterson wrote necrologies of the physicians of Lowell and vicinity from the year 1826 to 1898, and to him must be given credit for recording much of interest in connection with our society, including the sketches of the lives of many of the more prominent members.

There have been many distinguished fellows of the Middlesex North District Society, and it would be a great injustice to the memory of those fine and able men if some recognition were not given to their labors at this centennial celebration.

Among the many physicians who have practiced in this city is one who by his original views and fearless conduct was far in advance of his times as a medical practitioner and writer. Dr. Elisha Bartlett was a highly accomplished scholar and physician. He was an extremely popular medical teacher and a ready lecturer. He also attained great eminence as an author, and his published books and pamphlets, both professional and miscellaneous, are numerous. He held various professorships in the Berkshire Medical Institution at Pittsfield, the Medical Department at Dartmouth College, Louisville University and the medical college at Woodstock, Vermont.

It is an honor to the medical profession that one from its ranks was chosen to be the first mayor of this city. It was a mark of special distinction that this responsible trust should have been bestowed on Dr. Bartlett when only thirty-two years of age. Dr. Oliver Wendell Holmes, a lifelong and intimate friend of Dr. Bartlett, when speaking of his death remarked that his loss was a national calamity.

In 1824, two years before the incorporation of the town of Lowell, there came into this place a young

man possessing unusually promising traits of character. These and other excellent qualities were united in the person of Dr Elisha Huntington. He was an able physician of rare culture and scholarly attainments. As a family physician he enjoyed the confidence and high regard of a large number of families in this community, who retained his services as long as he lived. Charity to the poor was one of his marked characteristics. Dr Huntington, in presiding at the head of the municipal government, finished a career that has never been excelled in local history. In 1856 he entered for the seventh time on the duties of mayor. So long as the fame of this city shall survive, the public services of Dr Huntington will live on Lowell's records, and his name will occupy a prominent place in its history.

Prominent among the early physicians stands the name of John C Dalton. Dr Dalton was an ardent lover of his profession, and gleaned those acquisitions that enabled him to take high rank not only with his local medical associates but among the leading physicians of the Commonwealth. The entrance of a young physician into professional life in those days was somewhat different from the usual custom of later years. In some respects it was not unlike that of a minister receiving a call to serve a parish. Dr Dalton virtually received a call from the people of Chelmsford, and it was extended in the following manner. In 1818 Dr Wyman, who was then practicing at Chelmsford but had received an appointment as superintendent of McLean Asylum, was requested by the citizens of the town to appoint a successor. On his recommendation, Dr Dalton, then in his twenty-third year, began his practice.

An amusing incident, as related by Dr Dalton, occurred on his first coming to Chelmsford, the mother town of Lowell. Dr Wyman took him around to different parts of the town and introduced him to the leading families, speaking a good word in his behalf, for he looked very youthful as compared with Dr Wyman. In calling on one of the principal families, its head, a man remarkable for age and wisdom, after making a survey of the "young doctor" remarked that a physician would have to fill more than one graveyard before he had a chance to experiment on him. Notwithstanding the shock this remark made on the young Dr Dalton at the time, this family became one of his best patrons.

Very few men have had the distinction of having four eminent sons as did Dr Dalton. Two of them became noted physicians, and through the generosity and interest of one of the other sons a substantial sum, long known as the Dalton Scholarship Fund, was established for medical research at the Massachusetts General Hospital.

A bold and daring pioneer surgeon of this city who, through his explorations in uncharted surgical fields, before the discoveries of Louis Pasteur and Lord Lister, contributed much to medical science for the relief of suffering humanity was Dr Gilman

Kimball. When the Lowell Corporation Hospital was established, Dr Kimball was elected physician-in-charge. He was retained in this position for twenty-six years.

Dr Kimball was one of the first in the practice of ovariectomy in this country. There is no other operation known to medical science that early met with such decided opposition on every hand as did this branch of operative surgery. The mortality was large. At that time the whole number of surgeons in this country who had ever performed this operation was less than ten. Before Dr Kimball's death he performed ovariectomy in 300 cases. According to Dr Howard Kelly, of Johns Hopkins, Dr Kimball has the distinction of being the first surgeon to perform successfully the removal of the whole of the uterus based on a correctly established diagnosis. He performed this operation in 12 cases, with 6 recoveries. In 1842, he was elected to succeed the brilliant Dr Willard Parker, of New York City, — one of Chelmsford's gifted sons, — as professor of surgery in the medical college at Woodstock, Vermont, and in the following year he was chosen to fill a similar position in the Berkshire Medical Institution at Pittsfield, Massachusetts. His name will pass into history as one of the foremost surgeons of this country.

At this time, mention should be made of some of the leading surgeons and physicians of the latter part of the century just closed, who can still be remembered by many. One whose name is familiar to all is Dr Moses Greeley Parker. Through his generosity he made it possible for the people of this district to enjoy the best in music, literature and art, as well as lectures on travel, health and hygiene. As a benefactor to the society he left a fund to provide dinners at the meetings similar to the well known Cotting Lunch Fund of the Massachusetts Medical Society. Others are Dr John C. Irish, a leading and skillful surgeon, and his two apt and able pupils Dr Robert E. Bell and Dr Joe V. Meigs, who were eminently successful surgeons. Dr Francis C. Plunkett was a beloved family physician and an original staff member at St. John's Hospital, where he served actively and ably for many years. Dr George H. Pillsbury was a cultured medical gentleman, whose father, Dr Harlin Pillsbury, was one of the charter members of this society.

One of the society's most energetic members during the last years of the century, who through his clear vision and forcible speaking was able to unify the profession in matters calling for firm and advanced action, was Dr J. Arthur Gage. In 1930 this society tendered to Dr Gage on his retirement a farewell banquet in testimony to his great worth and value to the community that he had served so well, for he was an acknowledged leader.

Finally, it may be said that the lives of these men who acquired, both in medicine and in other fields of civic endeavors, honorable distinction

among their contemporaries stand out as steps of progress in the growth of our society. Others equally deserving could be mentioned if time permitted.

The society has always had its quota of physicians in the Medical Corps of the United States Army and Navy. Not only in the Civil War and World War I have the doctors of Middlesex North District Medical Society taken an active part, but in the midst of World War II this society is well represented on all war fronts. We are proud of their work and the spirit that carries them on. If it were possible they would be here with us tonight. Since this cannot be, our earnest wish is that our prayers will be answered and that these young men may come

back to us safely. On their return after this conflict may they find that our association is appreciative in full measure of their unselfish efforts and the un-failing sacrifices that they have made. Furthermore, not only does the society know their true worth, but the wounded and sick soldiers know its members' skill. They also have felt the warmth of heart and sincerity of our profession.

When, in the course of time, another century of this society's existence shall have passed into history, the men then taking our places, even with their advances in the knowledge of medical science, can surely take an honest pride in the efforts, experiences and accomplishments of the physicians of the century just closed.

EARLY RISING AFTER SURGICAL OPERATIONS

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THE question of when a patient should arise following an operation is one concerning which there has for many years been considerable divergence of opinion. There has been an increasing tendency to get patients out of bed early, but few surgeons, particularly those of this country, have advocated that patients walk from the operating table or become ambulatory twenty-four to forty-eight hours postoperatively. Surgeons who have adopted this routine claim that all postoperative complications such as pneumonia, wound infection, thrombosis and embolism are less frequent than they are in the mobilized patient. Shortly after the turn of the century, largely owing to the work of Ries,¹ of Chicago, and Kummell,² of Hamburg, early post-operative rising had many advocates, but this routine gradually fell into disrepute until recently.

In 1937, Kimbarovskiy³ reported on 551 cases. Of 71 patients operated on for hernia of the linea alba, all walked from the operating table and 96 per cent were discharged not later than the seventh day after operation. Of 124 patients with inguinal or femoral hernias, 67 per cent walked from the operating table and 29 per cent arose on the following day, 94 per cent were discharged not later than the eighth day after operation. Of 210 patients with chronic appendicitis, 84 per cent arose on the following day, 79 per cent were discharged not later than the seventh day after operation. Finally, of 146 patients who had a gastric resection for ulcer, 63 per cent arose on the second hospital day and 26 per cent on the third, 42 per cent were discharged not later than the ninth day after operation. Kimbarovskiy is convinced that the incidence of post-

operative pneumonia, wound infection, thrombosis and embolism is lowered and that the incidence of hematoma and wound disruption is not increased in such patients.

In a subsequent paper he⁴ states that in a series of 1600 patients handled in this manner, the incidence of thrombosis and embolism was only 0.2 per cent. In the same paper he reports concerning experiments with 30 dogs. In all, the abdomen was incised in the midline and the stomach was incised. Half were kept recumbent and half were allowed complete movement, equal numbers of each group being killed on the fifth, seventh and ninth days. The scars in the stomach and abdominal wall were examined microscopically, those of the stomach were identical in both groups, whereas those of the abdominal wall showed much better healing in the active group than in the immobilized group.

In 1940, Niedeggen⁵ published an account of 1646 patients who were induced to leave their beds within twenty-four hours of operation if they had been ambulatory before it was performed and if they did not have a high fever. On the morning after operation, a nurse raised the upper part of the body from the pillow and another swung the legs over the edge of the bed. The patient was assisted to his feet and walked about the room for several minutes, being supported on both sides, and then was helped back to bed. This was repeated six hours later. On the second day, most of the patients were attended with little difficulty and many of them had their meals at a table. By the third or fourth day, little was required in the way of special care, and on the fifth or sixth day, it was not unusual to see patients walking in the garden or making themselves useful about the hospital. If there was marked exaggeration of

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wound pain, it was almost always due to an incorrect technic in getting up or to dressings so applied that pressure or traction resulted. In the entire series the incidence of thrombosis and phlebitis was 0.5 per cent, and 0.35 per cent of these patients had evidence of embolism. The operative mortality was 0.18 per cent, and not a single case was lost because of a pulmonary infarction. The types of operation are not given, but it is stated that of 51 patients who underwent gastric operations only 1 had a postoperative bronchitis and none had a subsequent pneumonia.

In 1938, Campeanu⁶ reported the end results in 1300 cases in which the patients either walked away from the operating table, if local anesthesia had been used, or arose from their beds as soon as paralysis had disappeared, if spinal anesthesia had been employed. The most frequent operations were as follows: appendectomy, 682 cases, phrenectomy, 165 cases, herniotomy, 126 cases, gastroenterostomy, 42 cases, gastric resection, 33 cases, resection of adhesions, 32 cases, and cholecystectomy, 28 cases. The operative mortality was 0.23 per cent, and not a single patient had a complication that could be attributed to early rising. Certain patients who had had an appendectomy or herniotomy left the hospital on the day of operation, and the majority had left by the third or fourth day, returning on the seventh day to have the stitches removed.

In this country, Leithauser and Bergo,⁷ in 1941, reported 436 cases in which the patients got out of bed soon after operation and were permitted to be ambulatory. The majority (370) of these patients suffered from acute or chronic appendicitis without evidence of spreading or generalized peritonitis. In the remaining patients the three most frequent operations were cholecystectomy (18 cases), herniorrhaphy (9 cases), hysterectomy (7 cases) and other pelvic procedures (6 cases). In the cases of appendectomy, the average number of days of confinement was 1.5 days and the average hospital stay 2.3 days. For the other cases, the figures were 1.9 days and 8.9 days, respectively, and the patients who were active on the first day had the most favorable convalescences. There was a single fatality due to a massive hemorrhage from jejunal ulcers, on the seventh postoperative day. Otherwise, there were no complications such as wound dehiscence, hernia, pneumonia and thrombophlebitis. These authors believe that early rising and graduated ambulatory activity increase the rate and depth of breathing and the tone and use of skeletal muscles, thus improving the circulation in the pulmonary, systemic portal and lymphatic systems, and that they probably promote the return of normal function of the vital organs and aid elimination through the kidneys.

Charbonnier⁸ starts his patients with deep breathing exercises and movements of arms and legs in bed during the period before rising, beginning as

soon as the patient has come out from the narcosis. His patients are never allowed to rise before the third postoperative day and are usually allowed to do so on the fourth postoperative day. In some cases they are kept in bed until the fifth day. In a series of 408 patients who underwent laparotomy there were only 17 who had postoperative complications, practically all these complications were minor, and none could be attributed to early rising. There was no case of evisceration or of pulmonary embolism, and there were no deaths.

Harild⁹ is opposed to early rising after laparotomy, chiefly because of reduction of the minute volume of the blood in connection with operation. In support of his position, he has made a study of the minute volume in patients who have undergone laparotomy for one of several conditions and in those on whom extra-abdominal operations have been performed. The types of laparotomy represented are appendectomy, laparotomy with ventrosuspension of the uterus, colostomy, exploratory choledochotomy and ventral herniotomy. Two extra-abdominal operations represented are radical extirpation of the breast and arthrotomy of the knee for a lesion of the meniscus. The minute volume was reduced after operation by 30 to 35 per cent, even in cases in which there were no clinical signs of circulatory disturbance. In cases with primary shock, the decrease was even more marked. In most of his cases there was little or no change in the minute volume on the first day after operation, the most marked changes occurring two or three days after it. He also notes that no clinical signs of cardiac deficiency were determinable, indicating that the cause of the changes in minute volume must be in the periphery. On the basis of these findings, Harild concludes that even though operation induces an increase of oxygen consumption there is a reduced minute volume, and that the increased need of the tissues for oxygen must be satisfied by way of an increased discharge of oxygen from the blood. On the basis of these findings he believes that it does not seem justifiable to permit patients to leave their beds after laparotomy, at a time when there is partial circulatory insufficiency.

Lindhart¹⁰ and other investigators have found that the transition from the supine to the sitting or standing position induces a reduction of the cardiac minute volume, and the experiments of Asmussen, Hohwu, Christensen and Nielsen¹¹ published in 1939, show that the circulation in the passive standing position must be looked on as actually insufficient. In this position, a considerable amount of blood, up to 500 cc., accumulates in the lower extremities. They believe that patients should lie abed until the circulatory deficiency has run its course, which requires from five to ten days and sometimes longer, depending on the gravity of the operation and possibly the type of anesthesia. Since a similar study was not conducted on those who arose early,

these findings can only be properly interpreted as showing what happens in the quiescent postoperative patient

Lerthausen,¹² in studying the vital capacity of 202 patients subjected to early rising, made readings each day in the lying, sitting and standing positions before and after surgical procedures on the abdomen. After early rising, the vital capacity returned to normal in half the prescribed period, convalescence closely followed the improvement in vital capacity. He believes that coughing exercises in the standing position are specific therapy for the rales and possible mucous plugs that may be present following operation.

In a review of the literature, Newburger¹³ notes the unfortunate experiences with early postoperative activity when coarse suture material and running stitches were used in closing the abdomen, many case histories ended with the notation, "On the tenth day they returned to the hospital with their guts in a napkin."

* * *

The patients who occasionally became ambulatory, and even violent, immediately after operative procedures as a result of accident or intercurrent disease and suffered no ill effects stimulated my interest in the possible advantages of early rising.

It was decided to allow young patients who were in good physical condition and who had undergone simple appendectomy to leave their beds as soon as they felt able. This usually occurred on the third or fourth day after operation. After a few months' experience, this same type of patient was urged to arise even earlier. Most were apprehensive and had to be assisted and encouraged, and it was with real trepidation that they took their first steps. These patients were not premedicated before becoming ambulatory, nor were they given lengthy encouragement. The nurses merely entered the room and requested the patient to rise and offered their assistance. Those who objected, a small percentage, were not forced to rise, but were encouraged again the next day and told that it was better for them to be out of bed early. Once up, they seemed particularly pleased in their ability to get along, and it was not difficult to keep them ambulatory. They were allowed to stay up for half an hour in the morning and half an hour in the afternoon. The period was lengthened each day, until on the fourth day the patient was in bed for only a short period in the morning and another in the afternoon. Emphasis was placed on the importance of walking. The patients were not merely moved from their beds and allowed to sit in chairs.

During the first day, the patient was usually rigid and apprehensive about moving and did not enjoy the procedure. On the second day, however, there was evidence of increased ability to move around.

By the fourth day the patients walked with comparative ease and could be found reading, lounging about or taking short walks without hesitation. Occasionally they reached this stage on the third postoperative day.

This method of treatment was gradually extended to include most postoperative patients except those too ill as a result of severe infection, previous disability or unusually severe postoperative reactions.

In patients subjected to more extensive procedures, such as cholecystectomy and hysterectomy, the routine was modified and they were allowed out of bed for ten minutes on the morning of the first postoperative day and again in the afternoon. They were occasionally given an opiate before rising. It was not until the third or fourth day that they stayed up for an hour at a time. Of the latter group, 20 per cent were unwilling to leave their beds until the second or third day.

The operative wounds in these cases were closed in a variety of ways. In all of them tissues were accurately approximated and bleeding points ligated. For a few years, silk was used to repair the fascia. At present, silk and fascia are being utilized in the repair of hernias, and other abdominal incisions are routinely closed with continuous No 0 chromic catgut to the peritoneum, interrupted No 1 chromic catgut to the fascia, No 000 chromic catgut to the subcutaneous tissue and black silk to the skin. The suture material used for vaginal plastics is No 0 or 1 chromic catgut. In upper abdominal longitudinal incisions, after suturing the peritoneum in the usual fashion, the rectus muscle is retracted. Almost invariably the transversalis fascia is found to be gaping in the superior half of the incision. It is impossible in most cases to close the peritoneum and transversalis fascia accurately with a single row of sutures, and many postoperative hernias may arise from failure to recognize this fact. In one follow-up of 393 patients operated on for gall-bladder disease, 12.9 per cent developed incisional hernias.¹⁴

In the present series of 823 patients who were out of bed on the first to third postoperative day (Table 1), there were no serious complications due to their early mobility.

These patients are instructed to return to the office for their first checkup in four to six weeks after operation. At the end of three months, another examination is made. If they are normal at that time, they are dismissed but are told to return if anything unusual occurs. Since many of these patients are from surrounding towns, the referring physicians usually make the succeeding examinations.

The following four complications have occurred. One patient, on whom a cholecystectomy was done, appeared normal at the first examination but later his physician stated that the operative wound was bulging and instructed him to wear a belt. Another patient, operated on for a recurrent inguinal hernia,

developed a thin area in the upper third of the operative wound six months after leaving the hospital. Protrusion does not exist at present, but it seems likely he will have a recurrence. A pulmonary infarct into the lower left lobe occurred in an obese male on the seventh day after he had been operated on for a gangrenous appendix. Recovery was complete. The fourth patient, admitted with a ruptured

ate oozing from the gall-bladder bed, it subsided promptly. Five grams of sulfanilamide powder was scattered widely throughout the operative area and a drain was inserted to the foramen of Winslow. The peritoneum was closed by continuous No. 0 chromic catgut, as was the transversalis in the upper portion of the wound. Three silk stay sutures were inserted, the fascia was closed by interrupted No. 1 chromic catgut, and black silk was used for the skin. The operation began at 12:45 a.m. and was completed at 1:20 a.m. The patient left the table in good condition.

When seen the following morning the patient appeared

TABLE 1 *Types of Operation in Patients Submitted to Early Rising*

TYPE OF OPERATION	YEAR								TOTAL No OF CASES
	1937	1938	1939	1940	1941	1942	1943	1944	
Appendectomy	56	50	57	33	58	82	71	74	481
Herniorrhaphy	—	—	—	—	—	3	1	2	6
Incisional	—	—	—	—	—	18	24	38	106
Inguinal	—	—	—	12	14	1	3	2	10
Femoral	—	—	—	—	4	10	13	22	57
Cholecystectomy	—	—	—	—	12	—	—	—	—
Abdominal operations for uterine displacement or disease of its appendages or both	—	—	—	4	5	10	18	28	65
Abdominal hysterectomy	—	—	—	—	5	3	16	14	38
Vaginal hysterectomy	—	—	—	—	—	—	7	3	10
Anterior and posterior colporrhaphy	—	—	—	—	—	4	10	12	26
Lysis of adhesions for intestinal obstruction	—	—	—	—	—	1	3	2	6
Suprapubic prostatectomy	—	—	—	—	—	—	1	2	3
Suturing of perforated duodenal ulcer	—	—	—	—	—	—	—	2	2
Cesarean section	—	—	—	—	—	—	5	6	11
Nephrectomy	—	—	—	—	—	—	1	1	2

ectopic pregnancy, ran an uneventful course until the eighth postoperative day, when she began to complain of pain in the calf of the right leg. Local tenderness, swelling and a positive Homans's sign were present. The thrombophlebitis remained localized, although slight swelling of the ankle persisted six months later.

All these patients were out of bed within twenty-four hours.

CASE REPORTS

CASE 1. J. C. (47706), a 72-year-old man, was admitted to the Milford Hospital on January 21, 1944, with a history of acute upper abdominal pain starting 36 hours previously. He was seen by his physician, who gave him 16 mg. of morphine, which brought partial relief. The following morning he was having chills and vomited repeatedly. He was again given morphine and experienced some relief. During the day he became progressively worse and was admitted to the hospital that evening.

On examination he appeared ill and uncomfortable. The temperature was 100.2°F, the pulse 94, the respirations 28, the blood pressure 140/76, and the white-cell count 21,400. The heart sounds were of good quality, with an occasional extrasystole. The chest was hyper-resonant, with many dry rales throughout both lungs. There were spasm and rigidity in the right upper quadrant of the abdomen, with maximum tenderness at a point 4 cm. lateral and somewhat superior to the umbilicus.

The diagnosis of an acutely inflamed gall bladder was made. The patient was given 5 per cent glucose in normal saline solution intravenously. After receiving 1500 cc., he was taken to the operating room with the drip still running at a rate of 60 drops a minute. Under nitrous oxide, oxygen and ether, a right upper rectus muscle-splitting incision was made. When the abdomen was opened, a swollen, tense, thick-walled gall bladder adherent to surrounding structures was found. It was freed by sharp and blunt dissection and walled off. An incision was made 1 cm. from the liver edge on the anterior surface of the gall bladder. It was deepened until a line of cleavage was made out, and the dissection was carried downward on the medial and lateral surfaces until the gastro-hepatic omentum was reached. This was carefully dissected, exposing the cystic duct and artery. They were doubly ligated and the gall bladder was removed. There was moder-

cyanotic. The respirations were audible outside the room. There were many moist rales throughout both lungs. A diagnosis of so-called "massive collapse" was made. The patient was placed on his feet, instructed to cough, walked a few steps and returned to bed. The cyanosis disappeared and the patient breathed comfortably, with but a few moist rales remaining. From then on, the postoperative course was uneventful. He was out of bed and walking each morning and afternoon. On the 4th postoperative day his general condition was good and he was eating well. He was discharged on the 6th day. At the last postoperative checkup, made on June 15, the operative wound was firm and nontender and gave no evidence of hernia.

CASE 2. H. W. (46869) a 47-year-old, obese woman, was admitted on September 14, 1944, with a history of having been under treatment for the last 2 years for menopausal symptoms. Five weeks previously, she began to bleed vaginally. One week before admission her physician examined her, stated that she had a fibroid uterus, and advised operation.

The general physical examination was essentially negative. On bimanual examination, the fundus was palpable 2 finger breadths above the symphysis. It was smoothly irregular, slightly tender and movable and filled both vaults. The cervix was hard and smooth but not otherwise remarkable.

On September 16, under nitrous oxide, oxygen and ether, a supravaginal hysterectomy was done after the manner of Curtis.¹⁵ During the first 24 hours the patient received 1000 cc. of 5 per cent glucose in normal saline solution and 2000 cc. of 5 per cent glucose in distilled water. She appeared comfortable on the morning after the operation. She was given 16 mg. of morphine and half an hour later, with one nurse lifting her feet and another supporting her shoulders, she was placed in a sitting position on the side of the bed. After a short interval, she was helped to step to the floor and was assisted in walking about the room. She sat in a chair for 10 minutes, walked back and was helped into bed. This process was repeated twice a day. On the 2nd and 3rd postoperative days she had a few gas pains with no visible distention. By the 5th day, with a nurse lending slight support, she was walking with assurance and appeared quite comfortable. She was discharged on September 25 with the wound healing by first intention and with no evidence of infection.

Her physician did the postoperative checkups and reported that she had had an uneventful convalescence.

CASE 3. M. N. (47867), a 26-year-old woman, was admitted on February 17, 1944, at term and in active labor. The head was not engaged. She was given a test of labor lasting

for 14 hours, but the head still failed to engage. She was then moved to the operating room for cesarean section.

Under nitrous oxide, oxygen and ether, a low midline incision was made. The peritoneal reflexion of the bladder was turned downward, and retractors were put in place. A transverse incision was made through the lower uterine segment. Unusually severe bleeding occurred from the uterine walls and was controlled by clamps. A living male child was extracted and 0.2 cc of Pituitrin was given intravenously. When the uterus began to contract, the placenta was removed. The incision in the uterus was closed by an inner layer of No. 1 chromic catgut sutures and an outer layer of interrupted sutures. Peritoneal reflexion was restored to cover the suture line. The pelvis was wiped out and the abdomen closed in layers, using No. 0 chromic catgut for the peritoneum, No. 000 chromic catgut for the subcutaneous tissue, No. 1 chromic catgut for the fascia and black silk for the skin. The patient left the table in good condition. Postoperatively she was given 1500 cc of 5 per cent glucose in normal saline solution, 11 mg of morphine as needed to relieve pain and 1 cc of ergotrate every 4 hours intramuscularly until she was able to retain tablets by mouth.

The following morning she appeared in good condition and was assisted out of bed, walked a few steps and sat in a chair for 10 minutes. This process was repeated each morning and afternoon, the ambulatory periods becoming longer as her strength returned. The temperature for the first 3 days did not go above 100°F, and from then on it remained normal. She was instructed to be active while in bed and had only slight abdominal distress for the first 3 days. The sutures were removed on the 8th day. The wound was clean and firm, and as the patient's general condition was good she was able to get in and out of bed with slight assistance and had no difficulty in walking. Her appetite was good, and she was allowed to go home.

A postnatal checkup 8 weeks later revealed no evidence of prolapse. The abdominal incision was firm, and there were no abnormalities.

CASE 4 H. B. (43642), a 56-year-old man, was admitted on May 31, 1942, with two large, painful inguinal hernias and a history of asthma and chronic bronchitis. He experienced respiratory distress if kept in a recumbent position for any length of time because he could not clear the mucus that accumulated in the bronchial tree.

On June 1, under nitrous oxide, oxygen and ether, a bilateral repair was done. After dissection of the hernial sac and return of its contents into the abdominal cavity, the sac was ligated at its base by interrupted sutures. A portion of the conjoint tendon, fascia and muscle of the internal oblique was attached to the inguinal ligament by interrupted silk sutures and by a strip of fascia taken from the external oblique, whose medial attachment to the symphysis was not disturbed. It was impossible to secure fascia-to-fascia approximation without placing sutures under tension, so that, in the upper third of the repair the muscle of the internal oblique was attached to the inguinal ligament. The defect in the external oblique was repaired by silk, the subcutaneous tissue was approximated by No. 000 chromic catgut, and black silk was used for the skin.

The patient was out of bed the following morning, walked about the room and spent considerable time in a chair. He required 1 cc. of 1:2000 Prostigmin on the 2nd and 3rd days for relief of abdominal distention. His chronic cough was only partially controlled by codeine. He was unusually active during the 11 postoperative days spent in the hospital.

His physician reported that there was no evidence of recurrence when he was last seen 1 year after the operation.

CASE 5 C. C. (46361), a 71-year-old, well developed but poorly nourished woman, was admitted on July 13, 1943, with a history of vaginal prolapse of 4 years' duration causing increasing discomfort and disability. She consulted her physician, who advised surgery.

The general physical examination was essentially negative, and the findings were consistent with the patient's age. There was complete prolapse of the uterus without ulceration of vaginal mucous membrane or cervix.

On July 15, under nitrous oxide, oxygen and ether, vaginal hysterectomy was done, following the technic of Adams.¹⁵

The 2nd day after the operation she was helped out of bed and walked a few steps. She was up each morning and afternoon for 10 minutes. By the 7th day she was walking with slight assistance and remained in a chair for an hour at a time, although she complained of occasional discomfort in the perineum. There was a rather profuse vaginal discharge, which cleared up slowly, and she chose to remain in the hospital until it was practically gone. She was discharged on August 7.

Her physician reported that her condition has remained excellent, with no evidence of prolapse.

SUMMARY

The dangers of prolonged postoperative bed rest, particularly in the obese and aged, are becoming more generally recognized, and there appears to be a favorable clinical response to early rising.

On the basis of a review of published cases and personal experiences, it seems safe to allow patients out of bed within twenty-four hours after operation in the majority of cases.

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MEDICAL PROGRESS

THE PRESENT STATUS OF ANTIMALARIAL DRUGS

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IN RECENT years much has been learned concerning the use of antimalarial drugs. The significant changes that have occurred will be discussed in the following paragraphs.

ATABRINE

Pre-Pearl Harbor Status

At the beginning of 1942, there were a large group of clinicians who had had ten years' practical experience with atabrine (quinacrine, *USP* mepacrin *BP*). Many of these were enthusiastic about the drug, not only because it provided an alternative drug for the treatment of malaria, but because they believed that it had definite advantages over quinine in the therapy, and certainly in the so-called "suppression," of malaria. If these clinicians hesitated to advocate its adoption in complete supersession of quinine, it was because quinine had a brilliant record of three hundred years' service in the treatment of malaria, because the advantages of atabrine over quinine were quantitative rather than qualitative and because it was thought possible, even if not probable, that chemists would soon synthesize some drug that would surpass atabrine in its antimalarial action. There was another reason, a political and economic one: atabrine was for many years manufactured only in Germany, whereas in several malarious countries—for example, India—quinine and the other cinchona alkaloids were already local products, and in others cinchona cultivation was recognized as possible and was being planned. Other physicians, although admitting the efficacy of atabrine, did not share the enthusiasm of their colleagues and did not believe that its introduction constituted a real advance. Still others actively opposed its use and appeared to take a delight in reporting untoward incidents that occasionally occurred during a course of atabrine therapy, often without distinguishing between its by-effects and the complications of the attack of malaria. Among this last group were the diehards who had an almost religious regard for quinine and considered it sacrilege to question its supremacy. These persons—unwittingly, of course—did a great disservice to progress, since much time had to be wasted in overcoming the strong opposition to the wider adoption of this drug, which they had aroused, among both the medical profession and the laity, by ill-advised public pronouncements.

Early Dosage Regimes

The dosage adopted in the initial clinical trials with naturally acquired malaria was necessarily arbitrary (Peter,¹ Napier and Das Gupta,² Napier, Butcher and Das Gupta³ and Green⁴). The majority of the patients in these and the later trials during the early years were Asiatics of small stature, and most of them were partially immune, so that, although the standard dosage adopted as a result of wider clinical experience was slightly larger than that used in the initial trials, it was of the order of a minimal dosage. This dosage was 0.1 gm. thrice daily for five days, occasionally extended to seven days, for therapy, and 0.2 gm. twice weekly for suppression.

Despite the satisfactory results of this therapeutic regime, it was noted that the action of atabrine on the parasitemia and fever was slightly less rapid than that of quinine, and for this reason quinine was sometimes recommended for the first two days of treatment, followed by the usual course of atabrine—for example, in the British Army routine (see below).

Pharmacologic Investigation

The pharmacologist was hampered in the early days by the inadequacy of the methods of determining atabrine in the urine, blood and tissues, he did show, however, that it appeared in the urine within a few minutes, whether the drug was given by mouth or intramuscularly, that traces could be detected there for some time, and that it accumulated in the tissues, but he did not provide any data to encourage the physician to modify his empirically adopted dosage routine.

When in 1942 Japan took Java, whence had hitherto come ten elevenths of the world's supply of quinine, the spotlight of medical research was naturally focused on atabrine, the only known synthetic substitute for quinine. After a little valuable time had been lost, on both sides of the Atlantic, by the not unnatural official hesitancy, in view of the doubts expressed by others, to accept atabrine at the value placed on it by the enthusiasts, the plans for its large-scale production were put into operation. At the same time intensive work on the pharmacology of atabrine was undertaken and important results were obtained at an early date. In a world now extremely plasma-level conscious

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†These workers gave 0.6 to 1.2 gm. in four days.

as a result of several years' experience with the sulfonamide drugs, it is not surprising that one of the earliest investigations was aimed at measuring the plasma level achieved by different dosage regimes and the minimum plasma level that is necessary to control the malarial attack. This work was aided by the fact that the methods of accurately estimating atabrine in the body fluids and tissues were much facilitated by the comparatively recently introduced photoelectric and other fluorimeters.

These studies, including that of Shannon et al.,⁵ led to some important observations, which can be summarized as follows:

The chemotherapeutic activity of atabrine is a simple function of the plasma concentration.

A large percentage — of the order of 90 — of the atabrine taken by mouth or given intramuscularly is fixed in the tissues, and about 3 per cent is excreted in the urine and 6 per cent in the feces in the first twenty-four hours. After administration is discontinued, the rate of excretion falls off rapidly, but traces are found in the urine for many weeks.

On the ordinary daily dosage of the earlier therapeutic regimes, the maximum plasma level is not attained for several days, but once a balance between the intake on the one hand and the rate of excretion and degradation on the other has been achieved, a fairly uniform level in the plasma may be expected. In a large group of persons taking atabrine daily, the mean plasma level is proportionate to the daily dose, but among subjects on the same dose the levels vary considerably, between extremes this variation may be fourfold — for example, from 30 to 120 gammas per liter after 0.3 gm. atabrine daily. In persons taking a regular daily dose, the general rule is that 40 per cent of the final level is reached at the end of the first day and 40 per cent of the deficit is made up each day subsequently, so that 90 per cent of the peak level is attained by the end of the fourth day. If, however, the dosage on the first day is doubled, this plasma level is attained at the end of the second day, and if it is trebled, this near peak is attained on the first day, and the peak level (for that particular dosage) can be maintained subsequently by the ordinary daily dosage. Conversely, when the drug is discontinued, the falling off in plasma level is at the rate of about 20 per cent daily for several days, but traces of atabrine are still present even after eight weeks.

In the suppressive regime of 0.4 gm. weekly, it has been found that the peak level of between 8 and 15 gammas is obtained about the end of the fourth or fifth week, however the dosage is divided, but that by increasing this to 0.6 gm., given in six doses, a level of the order of 15 to 30 gammas, with a mean above 20, is reached within the same period.

The behavior of atabrine is thus in sharp contrast to that of quinine (see below), which appears very early in the blood in relatively much higher concentrations, reaches its peak concentration in about four hours, and falls far below the therapeutic level by the end of twenty-four hours.

The plasma concentration of atabrine necessary to effect a clinical cure in malaria varies both with the host and with the strain of parasite, but it is generally concluded that a minimum level of 30 gammas is required. For suppression, a breakthrough* does not usually occur when the plasma level is above 12 gammas.

Clinical Experience

Field experience with totally nonimmune members of the British, Australian and American fighting forces, who were on the average considerably heavier and better nourished than the often partially immune Asiatics who had formed the bulk of the clinical material on which the earlier dosage regimes had been calculated, soon showed that these dosage regimes were inadequate from the point of view of both treatment and suppression. It also confirmed the opinion held by many of the earlier workers that the importance of the by-effects of atabrine therapy should not be overemphasized, and indicated that these by-effects are less likely to occur in better nourished persons, that some of them can be obviated by such simple measures as taking sodium bicarbonate or glucose at the same time, that most of them — for example, the gastrointestinal disturbances and the mild psychoses that sometimes follow the early doses — frequently do not occur later during the course when some tolerance for the drug has been established (Green⁶) and that they are therefore not an indication for discontinuing the drug altogether, nor even, except in rare cases, for modifying the dosage.

Dosage Revision

The advisability of increasing the dosage of atabrine thus became obvious, and the data that had meanwhile been accumulated made it possible to introduce a rational regime in place of the earlier empirical one. The most important modification that the pharmacologic investigations had indicated was the principle of "loading" the dosage during the early hours of treatment. This applies whether the drug is given by mouth or parenterally. The dosage recommended by the United States Army exemplified this principle. It prescribed the giving of 0.2 gm. of atabrine immediately and every six hours night and day during the first twenty-four hours, a total of 1.0 gm., and reverting to the three-times-daily dose of 0.1 gm. for another six days, that is, 2.8 gm. in all.

*A term indicating the development of clinical malaria during an established suppressive course.

For parenteral medication it is better to use the intramuscular route, since it has no disadvantages as compared with the intravenous one and is probably safer, by the latter route extremely slow administration is essential. In cases in which parenteral therapy is indicated, — for example, in the unconscious patient, — two injections of 0.2 gm. of atabrine in 5 cc. of distilled water are given into the buttocks, one on each side. Administration by the oral routine should be begun as early as possible, but, if for any reason this is delayed beyond six to eight hours, another intramuscular injection should be given and repeated every eight hours until oral therapy can be instituted. To ensure the necessary "loading," the oral dosage prescribed must be such that the total atabrine given in the first twenty-four hours amounts to 1.0 gm., and the usual 0.1 gm., thrice daily, is continued. (For smaller and less well nourished persons some modification of the dosage is necessary, but the loading principle should still be followed.)

This atabrine course does not by any means preclude relapses in natural infections of any of the three commonly encountered malarial species, but it is more effective in this capacity than is quinine or the other cinchona alkaloids, and it results in a longer initial period of freedom from relapses and wider spacing of subsequent relapses in benign tertian malaria, this is to some extent due to the slow rate of excretion of atabrine and its presence in the blood in appreciable quantities for several weeks. In malignant tertian malaria a second course of atabrine after an interval of ten days often results in a radical cure of this infection.

For suppressive therapy a daily dose of 0.1 gm. is given if this regime can be started not less than two weeks before the subject enters a malarious area, but if an earlier entry is likely, the loading principle should be achieved either by doubling the daily dose for the first week and continuing on the usual daily dose of 0.1 gm. or by giving a single loading dose of 0.6 gm. before commencing the ordinary regime (Medical Research Council recommendation).

So-Called "Practical Prophylaxis" in Malignant Tertian Malaria

There is no drug that acts as a true prophylactic in malaria and destroys or prevents the further development of the sporozoites injected by the mosquito. The failure of quinine to do this has been recognized for many years, and it has been repeatedly shown that nonimmune persons subjected to *Plasmodium vivax* infection during a suppressive course of atabrine, although they remain free from clinical symptoms while on the suppressive treatment, invariably come down with a clinical attack of malaria between the second and fourth weeks after they discontinue the suppressive regime. It has,

however, been shown that practical prophylaxis, at least against the South Pacific strains of *P. falciparum*, can be achieved, — that is to say, by giving 0.1 gm. of atabrine daily for two weeks before and twenty-three days after subjection to a heavy infection by this parasite, the subject is protected from any clinical manifestation of malaria, — and that after the drug is discontinued this freedom from clinical malaria lasts indefinitely unless the subject is reinfected. That this is only practical prophylaxis and not true prophylaxis entailing destruction of sporozoites is shown by the fact that early development of the schizogony cycle does actually take place, — as proved by blood-inoculation experiments, — but it does not reach the clinical threshold.

To summarize, it has been shown that in the administration of atabrine for both the suppression and the cure of malaria, by the adoption of more rational regimes, indicated by recent investigations, most of the disadvantages hitherto associated with its use can be overcome, and that in both capacities, and unquestionably in the former, it is the drug of choice. Given in suppressive doses it is apparently a practical prophylactic in *P. falciparum* infections of the South Pacific.

PLASMOCHIN

Plasmochin (pamaquine, *USP* pamaquin, *BP*) was introduced by Schulemann, Roehl and their co-workers (Roehl¹⁷) at Leverkusen in 1924 as a synthetic substitute for quinine, after preliminary screening experiments with *P. relictum* infections in canaries. It did not live up to the early claims made for it by its introducers, but it did find a place in the therapeutics of malaria. It was soon shown that by itself it was not a practical drug for use in the treatment of the malarial attack. It stopped the schizogony cycle and cured the clinical attack in both benign tertian and quartan malaria, but only when given in large and toxic doses, and even in these doses it did not affect the clinical attack or the schizogony cycle in malignant tertian malaria. On the credit side, however, it was found to destroy, or at least sterilize, the circulating gametocytes, particularly in malignant tertian infection, in small and perfectly safe doses — 0.01 gm. twice daily for three days. Although gametocyte destruction is not a measure that in any way aids the patient, it is in certain circumstances an important precaution as a prophylactic measure for the general population in a malarious country, and in this capacity plasmochin occupies a unique position, even today, because neither atabrine nor quinine achieves this. Further, it was found that although little was gained by adding plasmochin to quinine so far as the current attack of malaria was concerned, it was of value in reducing the number

of relapses in benign tertian malaria,* but here again only when given in doses that were toxic to the majority of the subjects, and so toxic to a few that the treatment had to be abandoned.

When atabrine was introduced, the assumption that this drug could be used instead of quinine in the quinine-plasmochin antirelapse regime was somewhat too readily assumed. It was believed that the toxicity of each drug was enhanced by its association with the other, so that the dosage of plasmochin was whittled down and it was given separately instead of coincidentally with atabrine. Claims for the relapse-preventing properties of the plasmochin-atabrine combination† were not of the same order as those made for large doses of plasmochin and quinine, but undoubtedly some of the aura that had been generated by the latter gathered around the former combination, and an exaggerated idea of the value of the addition of plasmochin to the course of atabrine was widely diffused through the medical literature. This impression was fostered by the adoption at the outset of the present war of the so-called "2525"‡ regime by the Royal Army Medical Corps and the similar quinine-atabrine-plasmochin regime of the United States Army Medical Corps, so that it came as somewhat of a surprise to many when the Army treatment regimes were revised and plasmochin was dropped altogether. This gave plasmochin a bad name that it had certainly not earned, and led to such statements by the ill-informed as "Plasmochin has proved a failure" and "Plasmochin has not lived up to its reputation." The fact was that the Army authorities realized that there were few circumstances in which there was much to be gained by destroying the gametocytes whose destruction could in any case be achieved by a smaller dosage of plasmochin, that the antirelapse properties of this small dosage were

at the best extremely slight in benign tertian and were nonexistent in malignant tertian infections and that it was not worth prolonging the treatment regime and risking toxic symptoms in the few persons who had an idiosyncrasy, for such questionable advantages. Plasmochin is still, however, the only drug that clears the blood of malignant tertian gametocytes¶ and in combination with other drugs prevents relapses in benign tertian malaria, or at least cuts them down to an extremely low percentage. One ought perhaps to return to the surer ground of the plasmochin-quinine combination and test the effect of a safe plasmochin dosage, that is, 0.01 gm thrice daily, given coincidentally with quinine, over a longer period, say ten to fourteen days.

But this is not all. James and his co-workers¹⁴ showed that by giving large doses of plasmochin (0.08 gm daily for three days and 0.06 gm for five, a total of 0.54 gm) before and immediately after infection with benign tertian sporozoites, practical prophylaxis could be achieved, although they failed to produce this effect consistently with smaller, even though still toxic, doses, namely, 0.06 gm daily for seven days. In the cases in which prophylaxis failed, the subjects had their first clinical attacks nine months after infection.

There is thus reason to believe that, although the practical use of plasmochin is limited by its high toxicity, it is in several ways a unique drug, in that it affects certain stages of both benign and malignant tertian parasites that are unaffected by the other antimalarial drugs now in use. It is hoped that, with plasmochin as an example, it will in time become possible to synthesize a quinolin derivative with the same therapeutic potentialities as plasmochin but without its limiting toxicity.

QUININE AND OTHER CINCHONA ALKALOIDS

Whereas the cinchona alkaloids have been in use for over three hundred years, the alkaloid quinine has occupied its special privileged position for less than a hundred years. The scientific basis for the choice of this alkaloid was probably sound, but the circumstances that placed it in such a position of dominance were unfortunate, for they led directly or indirectly to the development of a monopoly that had repercussions that have in turn proved disastrous to the outside world and to the monopolists themselves.

The climate in Java was such that it was possible to grow a particular variety of cinchona, *Cinchona ledgeriana*, which gave the richest yield of quinine, so much more easily than elsewhere that the large cinchona plantations in Ceylon, India, South America and elsewhere were eventually driven out.

¶The closely allied Cilonal, which has never been issued for general use, also achieves this but otherwise has no advantage over plasmochin and so possibly do some of the other recently discovered drugs.

*Sinton and Bird⁸ showed that when a course consisting of 0.10 gm. of plasmochin and 1.25 gm. of quinine daily for twenty-eight days was given to 20 soldiers with benign tertian malaria no relapses occurred, and that when the dosage of plasmochin was reduced to 0.06 gm daily in smaller subjects and the drugs were given for a total of seventeen days (with various intervals) to 15 soldiers only three relapses occurred. That is, in 35 cases there were three relapses, a rate of 9 per cent, compared with a rate of 77 per cent in a series of 111 cases in which quinine was given in the usual doses. Sinton, Smith and Pottinger⁹ also had no relapses in a series of 17 patients given 0.06 gm. plasmochin and 1.31 gm. of quinine for twenty-one days. All the subjects in these experiments and the controls were under military discipline and were kept under clinical and parasitologic observation for a minimum of two months, although this did not preclude the possibility of a late relapse, at least the controls showed a high percentage of relapse within these two months. In India a course of 0.04 gm. of plasmochin and 1.31 gm. of quinine for three weeks was given to all soldiers both British and Indian with a benign tertian infection, with highly satisfactory results in a group of over 3000 cases—so satisfactory in fact that in 1934 the convalescent depot at Kasauli where much important experimental work on antirelapse therapy had been done since 1924 had to be closed on account of the paucity of cases of relapsing benign tertian malaria. Since the fall in incidence preceded the adoption of atabrine, it was attributed by the Army authorities to plasmochin administration (Amy and Boyd¹⁰). Toxic effects were, however, not uncommon (Manifold¹¹).

†In 1933-1934, Bird¹² in a series of trials in India showed that by giving 0.01 gm. thrice daily for five days after the course of atabrine, the relapse rate in benign tertian infection was reduced to 50 per cent, as against 45 per cent for quinine with the same plasmochin dosage; the groups comprised 150 and 200 cases respectively. Gentzkow and Callender¹³ also effected a distinct although not spectacular reduction in the recurrence rate among military personnel in Panama by adding 0.01 to 0.02 gm of plasmochin to the atabrine course thrice daily for three to five days.

‡Two days of quinine five days of atabrine two days of rest and five days of plasmochin.

of business. The price of quinine was then raised to a level that made it difficult for the malaria sufferers in poor countries to afford the amounts of this drug that they needed.

It has long been appreciated that the other crystalline alkaloids of cinchona bark also have high anti-malarial properties, and an attempt has been made in several countries to introduce a mixture of cinchona alkaloids—for example, the total crystalline alkaloids of the bark of certain hardier cinchona trees, *C. robusta* and *C. officinalis*—for general use against malaria. This scheme was fostered by the Health Organization of the League of Nations. The main obstacles to the more general adoption of the mixed alkaloids were the conservatism of the medical profession and the vested interests of the cinchona planters. The result was that when the Java plantations were taken by the Japanese early in 1942, little progress had been made in the scheme for extending the cinchona plantations in any of these countries. Nevertheless, it was believed that the possibilities should be further explored, and as a part of the research program further studies in the pharmacologic and therapeutic properties of the cinchona alkaloids were undertaken.

Pharmacology

As noted above, the peak plasma concentration of quinine is reached within four hours of the oral administration of this alkaloid, but the concentration falls rapidly. This means that it is a useful drug for its quick action but that continuous administration is essential for the action to be maintained. After the routine administration of quinine—1.3 to 2.0 gm. daily in two or three doses—the plasma concentration reaches 3 to 10 mg. per liter and remains there.

The efficient therapeutic level varies for different hosts and for different species and strains of parasite, it is of the order of 3 to 5 mg. per liter but rises to 10 mg. for quinine-resistant strains, especially those of *P. falciparum*. It is, however, essential that this level be maintained for several days.

The rate of absorption and the levels of plasma concentration of quinidine and cinchonidine were found to be similar to those of quinine, but the rate of absorption of cinchonine appeared to be much slower and less complete. It was shown, however, that the absorption of cinchonine was actually as complete as that of quinine, but that its rate of degradation was much higher. As a result, the plasma level was only a fraction of that of quinine after the same oral or parenteral dose. On the other hand, the therapeutic activity of cinchonine was much greater than that of quinine, a plasma concentration of 0.3 mg. per liter maintained for four days being curative in benign tertian infections. The higher therapeutic activity of cinchonine thus fully compensates for the low plasma level, and the final result of the oral or parenteral administration

of equal doses of the two drugs is the same, with perhaps a slight clinical advantage for cinchonine on account of its lower toxicity.

Clinical Experience

The Madras (India) Cinchona Commission in 1867–1868 first reported that the actions of the four principal cinchona alkaloids, quinine, quinidine, cinchonidine and cinchonine, on “malarial fever” were equal. This observation was confirmed later by several observers, including Sinton and Bird.¹⁴ As a result of the renewed interest in this subject, further investigations were undertaken in the United States and Great Britain. All these confirmed the previous opinion that each of the other three crystalline alkaloids has approximately the same anti-malarial action as has quinine. Field experiments also showed that a totaquine* mixture consisting of about 70 per cent total crystalline alkaloids was as effective as quinine alone in approximately the same dosage. It was, however, noted that the disagreeable by-effects were more frequent with totaquine, and it was once again concluded that these were mainly caused by the amorphous alkaloids in the mixture. On the other hand, there was no evidence that any one of the crystalline alkaloids or any combination of them was more effective than quinine in preventing relapses, or that any of them would act as a true causal prophylactic.

Since the peak plasma level is reached so soon, an initial loading of the dosage is unnecessary, and probably inadvisable, in the treatment of Asiatics of small stature with quinine or the other cinchona alkaloids, but for nonimmune white troops the Army practice is to give 1 gm. thrice daily for two days and 0.67 gm. thrice daily for the next five days. I believe that this is only to be recommended in malignant tertian infections.

As a suppressive drug, quinine was used extensively in World War I by the British and French in Macedonia. Its practical failure in this role was attributed to the failure to see that the troops took the drug properly, since for many years before and after 1918 it had been used extensively in civil life in the tropics, in some cases with a considerable degree of success. Since Pearl Harbor, not much quinine has been available for use as a suppressive, but on the few occasions on which it was used it was not a conspicuous success. Its pharmacology makes this understandable, and since there is no reason to believe that any of the other alkaloids would be more active, it seems probable that in this capacity the cinchona alkaloids will have to give way to one of the synthetic drugs, atabrine or its successor.

To summarize, recent experience in the laboratory and field has made no material difference in opinions concerning the value of quinine and the other cin-

Totaquine is the name suggested by the Health Organization of the League of Nations for a standardized mixture of the alkaloids of cinchona. This is the official B.P. designation, the U.S.P. one being, totaquine.

chona crystalline alkaloids, although further scientific evidence has been provided to show that all the crystalline alkaloids of cinchona are equal in their antimalarial activity, and that a mixture of these alkaloids can be used as a completely efficient substitute for the single alkaloid quinine

OTHER SYNTHETIC ANTIMALARIAL DRUGS

Another line of investigation has been the search for new synthetic antimalarial drugs. Many such drugs have been synthesized, and some have been shown to possess antimalarial properties equal to and even greater than that of atabrine, but their superiority has been quantitative rather than qualitative, and up to the present no one has been found that does what atabrine does not do, namely, destroy the sporozoites or prevent relapses in benign tertian malaria

It is probable that if no better drug is found some of these will be manufactured and marketed after the war, but the authorities in the Allied countries have wisely decided that, in view of atabrine's background of fifteen years of laboratory and clinical trial, it would be foolish to change over to some other drug for the sake of apparent minor advantages, without the knowledge of its limitations that only long experience can provide

CONCLUSIONS

Prior to 1942, atabrine was looked on as a valuable addition to the armamentarium of the physician for the cure and suppression of malaria, but its place was certainly second to that of quinine. Recent work has shown that it is probably the most valuable drug in the fight against malaria

Despite the fact that quinine and the other cinchona alkaloids have had to take a place below atabrine on the antimalarial priority list, recent work has in no way questioned their efficacy. On the contrary, it has confirmed previous work regarding the antimalarial activity of all the crystalline alkaloids, and more especially that of a mixed alkaloidal preparation, which in some of the poorer malarious countries may, on economic grounds, still prove to be the drug of choice for the mass of the population

The strict limitations of plasmochin in the treatment of malaria have long been recognized, and recent experience has merely served as a reminder of these limitations. It is, however, the only drug that acts as a true causal prophylactic or actually prevents relapses in benign tertian malaria, albeit

in large and dangerous doses. These unique properties should be recognized and, in special circumstances, full advantage taken of them. Furthermore, it seems possible that by a modification of the formula of plasmochin a less toxic but equally efficacious drug may be synthesized. The discovery of such a drug will give man a weapon with which he will be able to control malaria not only in the individual but in the community. Although it is improbable that malaria will ever be banished by the use of drugs alone, with a drug possessing these properties it may be possible to control it in some communities where this was hitherto impossible, and in others to do so more effectively and at lower cost than would be possible by any other means. Until, however, such a drug is discovered no claim for man's mastery over malaria can be made

It will be surprising if the intensive chemical and medical research that is now being carried on in several countries does not lead to the discovery of a synthetic drug in which all the qualities of the known antimalarial drugs are combined with some unique ones of its own. Meanwhile, there are three valuable antimalarial drugs: atabrine, the cinchona alkaloids, including quinine, and plasmochin. Each has its own place in the treatment of malaria

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31281

PRESENTATION OF CASE

A forty-five-year-old hospital attendant was admitted because of an increasingly productive cough.

About one and a half years before admission the patient began to notice painless swelling of the finger tips and stiffness in the knees. The limitation of motion slowly progressed to involve the ankles, wrists, elbows and interphalangeal joints of the hands and feet. These joints were never red or hot. The stiffness was accompanied by dull constant pain, which diminished somewhat with use. Gradually the involvement of the upper extremities subsided, but the knees and ankles became very swollen and exquisitely painful and the limitation of motion progressed. There was still no redness or heat. Two months before admission he was advised to have his remaining teeth extracted. This he had done. About a month before entry, without chills, fever or chest pain, he developed a productive cough, which soon daily yielded 200 to 400 cc of whitish, non-blood-streaked phlegm. He also began to have night sweats two or three times a week. During the nine months before admission he had complained of dyspnea on exertion, which did not progress. His appetite had remained good, but during the previous one and a half years he had lost 15 pounds.

There was no history of gonorrhea or exposure to tuberculosis. For many years the patient had imbibed freely of rum.

Physical examination revealed an emaciated, moderately dyspneic, edentulous man in considerable discomfort because of painful legs. He showed definite gynecomastia. Expansion of the chest was symmetrical, and the chest appeared to be fairly emphysematous. Rhonchi and wheezes were heard over the entire chest posteriorly but were most pronounced at the bases. Tactile and vocal fremitus and resonance were normal. The abdominal wall showed considerably dilated veins. The liver and spleen were not enlarged. The knees, ankles, feet and all toes showed marked swelling, tenderness and pain on motion. The skin over these areas was tense, glossy and light pink. There was no redness or heat but marked hyperhidrosis. The patellas were definitely elevated and ballotable, and a fluid

wave could be obtained over the knee joints. The swelling over the legs, ankles and dorsums of the feet was firm and did not pit. The fingers and toes showed clubbing of an advanced degree.

The temperature was 99.5°F, the pulse 90, and the respirations 20. The blood pressure was 112 systolic, 80 diastolic.

Examination of the blood showed a red-cell count of 4,700,000, with 11 gm of hemoglobin, and a white-cell count of 10,500, with 77 per cent neutrophils. The urine was normal. The serum chloride was 95 milliequiv per liter, the prothrombin time 22 seconds (normal, 18 to 20 seconds), the protein 4.8 gm per 100 cc, the calcium 6.6 to 8.3 mg per 100 cc, the phosphorus 3.1 mg, the cephalin flocculation test + in forty-eight hours, the alkaline phosphatase 4.1 units per 100 cc, and the corrected sedimentation rate 17 mm per minute. The stool was normal. Synovial fluid drawn from the left knee was slightly cloudy and pale yellow, and most of it promptly clotted. It contained 100 white cells and 700 red cells per cubic millimeter (of the former, 20 per cent were polymorphonuclear cells and 80 per cent were monocytes) and 106 mg of sugar (serum sugar 136 mg) and 2.2 gm of protein per 100 cc. Repeated sputum cultures showed few beta-hemolytic streptococci, a few staphylococci and no pneumococci, spirochetes or other pathogens of significance. The Hinton test was negative. A 1:10,000 tuberculin test showed a 1.0-cm area of redness with a 0.5-cm central zone of induration. A bronchoscopic examination was negative, except for the presence of an increased amount of thin white secretion.

X-ray studies showed slight decalcification of the bones of the hands, arms, knees and feet. There was an extensive feathery periosteal proliferation involving the majority of the bones. This had the characteristic appearance of pulmonary osteoarthropathy. The chest films showed a homogeneous shadow of increased density with somewhat ill-defined margins in the axillary portion of the left upper lobe. No definite fluid level was seen. The diaphragm, heart and aorta appeared normal.

Throughout the patient's course in the hospital the temperature was normal except for an occasional low-grade fever, which rarely reached 101°F. The pulse was somewhat elevated, usually between 90 and 110, and the respirations were normal. He produced from 60 to 400 cc of white nonpurulent sputum daily. His appetite remained fair, and he lost no further weight.

After the second week he was given approximately 100,000 units of penicillin per day. Aspirin fairly well controlled his joint discomfort. A cephalin flocculation test repeated during the third week was +++ in forty-eight hours. The prothrombin time was 31 seconds (normal, 18 to 20 seconds). During the fifth week the calcium was 8.3 mg per 100 cc and the protein 6.0 gm per 100 cc. X-ray films of the chest repeated four and six weeks after ad-

*On leave of absence.

mission showed a rather marked increase in the size of the lesion in the left upper lobe on each occasion (Fig 1) The patient insisted that his joints were less painful and that he felt generally better The urine remained normal, except for a ++ test for urinary calcium (Sulkowitch test) The white-cell count rose briefly to 23,800, with 83 per cent neutrophils

He was given several whole-blood transfusions and was maintained on daily penicillin, Synkovite

The symptoms and signs in this case center around three systems — the lungs, the liver and the joints It would be nice if we could find a diagnosis to cover all three systems The chances are that we shall not be able to We might rule out some diagnoses right away and include others I think one can rule out pulmonary tuberculosis simply because the x-ray appearance is not characteristic and because the negative sputum and the past history are against it The patient undoubtedly had pulmonary



FIGURE 1 *Roentgenogram of Chest*

and Hykinone for two weeks On the thirty-first hospital day an operation was performed

DIFFERENTIAL DIAGNOSIS

DR JACOB LERMAN One point in the history worth commenting on is that the patient noticed painless swelling of the finger tips one and a half years before entry If that is an accurate observation, then we can date the beginning of clubbed fingers It is not infrequent, however, for a patient to mistake the terminal joint for the tip of the finger, so that the patient's statement, unless he was sure of it, may be a source of error I shall assume, however, that he had clubbed fingers beginning one and a half years ago

osteoarthropathy That diagnosis is given to us It was an extensive type of pulmonary osteoarthropathy He certainly had some form of liver disease He had a high alcoholic intake, dilated abdominal veins and gynecomastia, which are important in the diagnosis of liver disease The blood chemistry is also consistent with liver disease The prothrombin time was elevated, the serum protein was low, and the cephalin flocculation test was positive We presume that they looked carefully for varices of the esophagus, which were not found, unless they were so sure of the diagnosis that they deemed it unnecessary to look We may conclude that he had characteristic portal cirrhosis

As so often happens in these cases with longstanding pulmonary disease associated with liver

disease one has to include amyloid disease in the differential diagnosis. There is, however, a good deal of evidence against amyloid disease. In the first place, the liver and spleen were not enlarged. Enlargement of these organs is a common finding in amyloid disease. Furthermore, there is no mention of the Congo red test. If it had been done I assume that it was negative. If it had not been done then certainly they did not think much of this diagnosis. My first impression in reading the story was that this patient did not have amyloid disease.

Could he have had rheumatoid arthritis? The history is consistent with this diagnosis except for the onset of clubbed fingers one and a half years previously. I am inclined to believe that the joint symptoms were part of the picture of chronic pulmonary osteoarthropathy rather than ordinary rheumatoid arthritis. As to the nature of the lung condition itself, before we go farther, I should like to see the x-ray films, particularly those of the lungs.

DR GEORGE W. HOLMES: The changes in the periosteum are well marked and extensive. It is a characteristic picture. I believe that one can say, so far as one can see on the x-ray films alone, that the whole picture in the joints was due to pulmonary osteoarthropathy. There is no evidence of rheumatoid arthritis. The joint spaces are not narrowed. If he had had rheumatoid arthritis for one and a half years there should be more evidence in these films.

In the chest there is a lesion that apparently lies outside the bronchus. It does not seem to interfere with the passage of air through the bronchus because the lungs and diaphragm move normally. There is no mediastinal shift. Furthermore, so far as I can make out, there are no metastatic masses or enlarged hilar lymph nodes. The lesion is definitely lobulated and the margins are not distinctly seen, but there is no cavity. It is possible, even with a homogeneous picture like this, that the cavity is completely filled with fluid. I presume that every effort was made to demonstrate a cavity because of the history of having had his teeth extracted.

We have no evidence that the bronchus is obstructed. The location of the tumor is of some interest. Apparently it is in the midportion of the chest, within the lung. It does not seem to reach the pleura, except at this point. Of course it would be helpful if I could tell you whether it is benign or malignant, and if the latter, whether it is primary or metastatic, but I cannot.

DR LERMAN: Dr. Holmes has been of help in one respect. He agrees that there is no rheumatoid arthritis and that this part of the picture is part of the syndrome of pulmonary osteoarthropathy.

What is the possibility of pulmonary suppuration? The patient had symptoms following the extraction of teeth but did not have chills or fever, and the chest films did not reveal an abscess cavity. Consequently we do not have sufficient evidence to make a diagnosis of lung abscess. Moreover, the pul-

monary osteoarthropathy in all probability antedated the development of the pulmonary symptoms. I think one may say that pulmonary abscess does not play an important role here unless there was an abscess caused by the breakdown of a tumor. Similarly we can discard an encapsulated empyema. There is no previous history of pulmonary infection, nor did this process displace the mediastinal contents as it progressed. Certainly the patient did not have the characteristic chills and fever and was not so sick as one would expect him to be with an encapsulated empyema.

The major problem is to decide whether this was a benign or malignant tumor. The presence of chronic pulmonary osteoarthropathy of an extensive sort favors a malignant tumor of the lung rather than a benign one, although I have seen one patient with an adenoma of the bronchus who had an extensive pulmonary osteoarthropathy. The rapid spread during the course of observation favors the diagnosis of malignant tumor. The long duration of pulmonary osteoarthropathy does not rule out malignancy but merely means that the tumor was of a slowly growing type. It is somewhat unusual for a malignant tumor not to show by x-ray some evidence of its character. I should say that, by and large, bronchoscopy should have revealed something of the nature and origin of this tumor if it were malignant unless it was in such an awkward position that the bronchoscopist could not see it.

I should like to digress a moment to discuss the relation between malignant tumor of the lung, gynecomastia and osteoarthropathy. There are descriptions in the literature of malignant tumor of the lung, chronic pulmonary osteoarthropathy of a severe nature and gynecomastia. This happens to be a case in point. It would be nice to put them all together. We have assumed that gynecomastia in cases of cirrhosis of the liver is due to failure of the liver to conjugate the steroid hormones, particularly estrin. This results in excessive amounts of estrin in the blood. One may theorize further that excess estrin, or some other steroid, may reach the terminal portions of the bones and produce changes in the periosteum characteristic of pulmonary osteoarthropathy. We know that these steroids have definite actions on the calcium metabolism and on the deposition of matrix in the bone. Failure to neutralize the steroid hormones might explain clubbing in cases in which some form of liver disease is present, but what about those that do not have obvious liver disease? One possible assumption in these cases is that malignant tumors of the lung frequently develop necrosis and suppuration, which may produce amyloid changes in the liver and simulate the functional disturbance present in cirrhosis. I merely interject this as a possible explanation. At grand rounds this morning a patient of Dr. Chester M. Jones was presented who had pulmonary osteoarthropathy and diarrhea, the latter probably

associated with a deficiency state. Here again is an ideal setup for liver disease and the development of pulmonary osteoarthropathy on the basis of the mechanism just proposed. It would be valuable support for this theory if Dr Jones's patient had gynecomastia, but unfortunately he does not.

DR BENJAMIN CASTLEMAN The twenty-four-hour excretion of 17-ketosteroids was 7.6 mg corrected and 8.6 mg uncorrected.

DR LERMAN That is a normal range for a patient who is sick. This test does not tell us about the excretion of other steroids, particularly estrin.

Unfortunately there is no easy test for estrin compounds. It necessitates a good deal of biologic testing and little of it is done. Nor is there an easy test for the progestin compounds, which may be present in male urine.

The second question is whether this was a primary or a metastatic lesion. One might speculate on the possibility of a metastatic lesion from the liver. We know that the patient had cirrhosis, and portal cirrhosis is frequently a precursor of hepatoma. This might, therefore, be a metastatic lesion from the liver. There is, however, no mention in the record of an abnormal mass in the liver. The liver was not palpable. This is against the diagnosis of hepatoma. Moreover, it seems unlikely that a secondary lesion from the liver could have gone on for a year and a half without producing evidence of metastatic lesions elsewhere in the body. It is an unlikely but a plausible way of tying in all three systems.

I believe that this patient had a malignant lesion of the lung, most likely a carcinoma but possibly some form of sarcoma, associated with pulmonary osteoarthropathy of long standing, and an independent portal cirrhosis.

DR RICHARD H. SWEET The findings at operation are often of much less importance than the necessity for making an accurate preoperative diagnosis. This case was presented to me as one of lung abscess. I did not accept that diagnosis, but I should like to point out the importance of making sure.

This man was in such poor condition that I was in no haste to operate. It took a good deal of prodding on the part of the house staff to get me to consent to operate at all. You can readily see that in a patient in such poor condition it is essential to determine the type of procedure beforehand, if it were an abscess one could do nothing but make an incision and drain, whereas if it were carcinoma one would do an open exploration. I throw that in for what it is worth. I came to the conclusion, as Dr Lerman did, that it was carcinoma, and used the extreme degree of pulmonary osteoarthropathy in making the diagnosis. We performed a total pneumonectomy.

CLINICAL DIAGNOSES

Carcinoma of lung
Pulmonary osteoarthropathy

DR LERMAN'S DIAGNOSES

Malignant tumor of lung, probably carcinoma
Pulmonary osteoarthropathy, chronic
Portal cirrhosis

ANATOMICAL DIAGNOSES

Adenocarcinoma of lung
Pulmonary osteoarthropathy, severe

PATHOLOGICAL DISCUSSION

DR CASTLEMAN This was a large granular tumor through which many small bronchi traversed (Fig 2). There was, however, no obstruction to the large



FIGURE 2 Photograph of Cross Section of Resected Left Lung

bronchi, although one of the bronchi in the posterolateral segment of the upper lobe did contain a nodule eroding the mucosa, which suggests a bronchiogenic origin. It is interesting to note that the tumor crossed the septum and extended for a short distance into the apex of the lower lobe. Microscopically the tumor turned out to be a low-grade adenocarcinoma. We have found that adenocarcinoma of the lung rarely occurs at the hilus, as in this case, usually being located more peripherally than are the epidermoid and oat-cell cancers. There was also a small metastasis in the lower lobe.

This man died soon after operation, and at autopsy we found a large metastasis in one of the adrenal glands. The sections of the breast showed a rather extreme degree of gynecomastia. In this

connection Fried* has reported 4 cases of carcinoma of the lung with pulmonary osteoarthropathy and some endocrine disturbance, such as gynecomastia. He also found that in some of these cases the anterior portion of the pituitary gland was increased in size, and in some the eosinophilic cells were increased in number. In this case, however, the pituitary gland was of normal size, and although I did not really count the cells, there did not seem to be an increase in the number of eosinophilic cells.

DR LERMAN: How about the liver?

DR CASTLEMAN: There was no cirrhosis or any evidence of chronic disease. There was some central congestion and necrosis, which was probably terminal.

DR MARIAN W. ROPES: It is surprising how many patients with pulmonary osteoarthropathy come in with a diagnosis of rheumatoid arthritis.

DR CASTLEMAN: We examined some of the bones microscopically and found all stages of periostitis—from the radiating fibrillar strands out from the cambium or inner periosteal layer to osteoid formation and, finally, calcification and fusion with the cortex.

CASE 31282

PRESENTATION OF CASE

A sixty-seven-year-old, invalid woman was admitted to the Emergency Ward at midnight because of hematemesis.

About six years before admission the patient had an episode of severe hematemesis, and about four months before entry she had another. On both occasions she was admitted to a hospital and carefully examined. The source of the hemorrhages could not be discovered. Four hours before admission to this hospital she had vomited a large amount of bright-red blood with clots. She became weak and apprehensive. A physician gave her a "hypodermic." Three hours later she came to the hospital. She had had rheumatoid arthritis for many years, and for the past eighteen years had been completely confined to a chair-and-bed existence. In addition to the above-mentioned hematemesis she had had other episodes of vomiting small amounts of blood. She had had no epigastric distress at any time and had never noted tarry stools. For many years she had taken an occasional aspirin tablet, which caused no gastric discomfort. There had been no awareness of fever. During the previous six months she had become somewhat anorexic. She had lost a great deal of weight and had noted a gradual increase in the size of her abdomen. She developed a bed sore on the back about four months before entry and had also noticed occasional burning on urination and occasional incontinence of urine.

*Fried, B. M. Chronic pulmonary osteoarthropathy: dyspituitarism as probable cause. *Arch Int Med* 72:565-580, 1943.

Eighteen years before entry she had had all her teeth extracted. For years she had had hemorrhoids, which bled frequently.

Physical examination revealed an emaciated, pale, grossly deformed woman with stertorous breathing and in a clouded mental state. There was bright-red blood about the lips. The tongue was not atrophic, but there were a few varices along the edges. The skin was loose, thin and extremely pale. The scleras were white. There were severe flexion deformities of the joints, all the large joints except the hips being rigidly ankylosed. Fine and moist basal rales were heard over both sides of the chest, and diffuse wheezes over the entire chest posteriorly. The heart was normal. The aortic second sound was greater than the pulmonary. The abdomen was distended and contained a moderate amount of fluid. The liver and spleen were not felt. A deep decubitus ulcer lay over the sacrum.

The temperature was 97°F, the pulse 100, and the respirations 15. The blood pressure was 125 systolic, 65 diastolic.

Examination of the blood showed a red-cell count of 2,300,000, with 7 gm of hemoglobin, and a white-cell count of 11,500, with 95 per cent neutrophils. The urine was acid, with a specific gravity of 1.018, the sediment contained innumerable white cells, an occasional red cell and many bacteria. The stool was liquid and grossly bloody. The serum non-protein nitrogen was 27 mg per 100 cc, the fasting blood sugar 133 mg, the carbon dioxide 21.2 milliequiv per liter, and the prothrombin time 17 seconds (normal, 18 to 20 seconds). A urine culture showed abundant growth of *Proteus vulgaris*.

A whole blood transfusion was begun shortly after admission. At 9:00 a.m. she was responsive and recognized her friends. She had not vomited since admission and showed no other signs of active bleeding. At 3:30 p.m. on the first day the blood pressure had fallen to 80 systolic, 40 diastolic, and the pulse had risen to 130. The skin was cool and clammy, and the patient was disoriented. At about 11:00 p.m. on that day, after a low enema, she passed a large quantity of fresh and clotted blood by rectum. At 9:30 a.m. on the second day the blood pressure had returned to 110 systolic, 70 diastolic, and the pulse was 110. She was in profound coma, and the respirations were stertorous. There were coarse gurgling rales in the dependent part of the chest. The pulse became progressively more rapid and thready. At noon on the second day she vomited dark-red blood. The hemoglobin level at that time was 4 gm per 100 cc. She expired at 3:00 p.m.

DIFFERENTIAL DIAGNOSIS

DR CHESTER M. JONES: We are not favored by x-ray films in this case, and I do not know whether or not that is going to be a help to me. I have been

making notes and juggling figures wondering how I shall bet, but I am definitely far from certain. In regard to the varices, were they said to be telangiectases in the record?

DR BENJAMIN CASTLEMAN Dr Pittman, can you answer that?

DR HELEN S PITTMAN As I recall they were definitely dilated superficial vessels, not telangiectases.

DR JONES I believe that this patient had more than one disease, which is not at all infrequent in this age group. She had obviously had rheumatoid arthritis for many years. Many patients with rheumatoid arthritis are badly nourished, however, as a result of anorexia and loss of weight. Nutritional disturbances, such as hypoproteinemia, prolonged prothrombin time and so forth, are not rare, particularly if salicylates have been given. Furthermore, as our group here has seen, rheumatoid arthritis may be accompanied by changes in the liver, including those of amyloidosis. But it is difficult to see how this could precipitate a picture such as this woman showed. It seems to me that the rheumatoid arthritis is not of primary importance.

The patient gave a six-year story of vomiting, off and on, with two major hemorrhages and a certain number of minor hemorrhages before her final admission. She had no other symptoms of any sort until six months before she entered. At that time she had a different story, namely, one of an increasing loss of appetite and a gradual swelling of the belly, accompanied by marked loss of weight, in other words, there was more weight loss than the scales showed. There was compensation, in a sense, because of an accumulation of fluid in the abdominal cavity. It seems to me that we have to explain the repeated hematemeses and the recent ascites, for both of which we have evidence on physical examination as well as from the story.

What are the causes of vomiting blood from the upper gastrointestinal tract? They are all perfectly well known. It is just a question of which one of these fits the picture, particularly if we try to tie in the ascites. If she had an ulcer, it should have been picked up on one of the previous x-ray examinations. She had had two gastrointestinal series, which at least were said to have been done carefully, — the first one six years before entry, and the second one four years before entry, — and no ulcer was noted. The absence of an ulcer story, together with the failure to find an ulcer by x-ray examination after a careful search, is definite evidence against such a diagnosis, although it does not rule it out. We have had more than one case of a bleeding ulcer that was not found until demonstrated by autopsy or operation, but that is the exception. In these exercises, the proper thing to do is to try to make a logical diagnosis on the basis of the facts presented. I believe that duodenal, gastric or esophageal ulcer is unlikely.

Could she have had esophageal varices, secondary to cirrhosis of the liver and causing bleeding and ascites? If one asks the question that way, of course the answer is that she could have had them, but with such a diagnosis, it would be unusual for her to have lived six years after the first hemorrhage. In the younger age group, we do encounter repeated hemorrhages from esophageal varices due to portal hypertension, the so-called "Banti syndrome", but in the older group, it is unusual to have a six-year interval between the first hemorrhage and the final fatal hemorrhage. I think this is of some importance in an attempt to rule out esophageal varices based on cirrhosis. Incidentally, it looks as if I were talking myself right into a corner. She was x-rayed at another hospital four months before, and if she had had varices they would undoubtedly have been spotted at that time. I assume that nothing was found.

DR CASTLEMAN The only statement that we have with reference to the hospital visit four months ago is that the daughter said that no cause was found for the vomiting of blood.

DR JONES Esophageal varices that cause hemorrhage can occasionally be missed by a careful roentgenologist, but with the six-year story of bleeding it seems rather unlikely that they would have been missed if they had been looked for. At times they are not found simply because the x-ray examination is done in a routine fashion and the esophagus not studied, only the stomach and duodenum being examined as the possible sources of the bleeding. She did not have a palpable spleen or liver, but I think that this may have been because the abdomen was so distended that it was impossible to feel a slightly enlarged spleen or liver. At any rate, for the time being I think that we have to pigeonhole a diagnosis of cirrhosis, but I am sure that it cannot be ruled out.

We have next to consider carcinoma. As a cause of the hemorrhage six years previously this also is an unlikely diagnosis. It is possible, however, that she had carcinoma of the stomach secondary to a benign polyp. We have seen that combination occasionally, but it is an unusual clinical picture. A polyp of the stomach is notoriously silent, and it can be missed by x-ray examination, since it is sometimes difficult to see. Subsequently the polyp may become malignant. Could that account for the ascites? It could, if by that time the patient had a carcinomatous process that had gone through the serosa of the stomach, or if there were regional metastases, either to the lymph nodes or to the liver. So I believe that that has to be put down as a possibility.

Diaphragmatic hernia could perfectly well account for the bleeding, although she had had no symptoms suggestive of diaphragmatic hernia. One sometimes sees fatal hemorrhage from diaphragmatic hernia in old people, but usually there

are symptoms suggesting something around the esophagus or stomach. Furthermore, x-ray films had been taken recently, and they should have shown a diaphragmatic hernia if it had been present. Again, this diagnosis can be missed in routine x-ray studies, but I should think that, if a hernia had been the cause of the hemorrhage, it would have been a fairly large one and would have been noted on x-ray examination.

One thinks of gastritis as a possible cause for this picture, although there were no symptoms. When gastritis is the major cause of hemorrhage, symptoms usually accompany it. With malnutrition, it is not at all surprising to get changes in the gastric mucosa and some atrophy, but this does not imply that such changes were the cause of this patient's bleeding. There is one theoretical reason for gastritis that might be considered, namely, the administration of aspirin. The record states that the patient took an occasional aspirin tablet. If she had been given a dosage of aspirin as large as that frequently employed in this hospital for painful rheumatoid arthritis, one could properly consider the question of gastritis. Fatal hemorrhage from this source has been noted in isolated cases, but it is most unusual to have repeated hemorrhages for six years on the basis of a gastritis due to aspirin. Furthermore, I believe that if this were so there would be a note in the record stating that the patient had taken a lot of aspirin and that it had been discontinued. Symptoms would probably be noted as well. I doubt that the aspirin plays any great role in this case.

If we consider only these five possibilities, we still have no conclusive evidence to help make a diagnosis. There are other conceivable conditions, and I suppose that they might as well be mentioned. She might have had a telangiectasis of the stomach, a curious congenital type of disease that may result in repeated hemorrhages over a long period of time. The telangiectases may be in the mouth, in the gastric mucosa or in any other part of the digestive tract. I take it that the lesions on the tongue were not the type that one gets in multiple telangiectases. I do not believe that she had it.

She could have had abdominal apoplexy, in the sense that one may get massive hemorrhage from a slight erosion that is not caused by a typical peptic ulcer, in which event this hemorrhage may occur anywhere in the gastrointestinal tract and all the x-ray films may be negative. Usually, however, there are a local source of irritation, specific pain and a marked rise in pressure that produces massive hemorrhage. There is no evidence that this patient had hypertension of any degree, so there is no reason to assume that such a thing occurred.

The case boils down, then, to the consideration of ulcer, esophageal varices, cancer on the basis of

preceding polyp, diaphragmatic hernia and gastritis, as the only reasonable possibilities. It is fair to say that the ascites could have been on the basis of nutritional edema. One sees such a picture occasionally, and one is hard put to explain why it occurs only in the abdomen and not in the extremities. We know that the patient had malnutrition. The aspirin may be a red herring. The ascites could have been on the basis of cirrhosis of the liver or on the basis of carcinomatosis, with the primary focus in the stomach or possibly in the duodenum. It seems to me that when forced to choose between such possibilities I am inclined to select cancer on the basis of a previous polyp of the stomach, in large part because of the story of definite loss of appetite of six months' duration, obviously a new symptom for her since she talked about it. Apparently this represented a striking change, something more than rheumatoid arthritis. I believe that this is the most logical bet. If she had cancer, she may or may not have had metastases. She could perfectly well have had fluid in the abdomen due only to malnutrition, although the normal prothrombin time is definitely against it, it is likelier that there were metastases. The other possibilities are cirrhosis with esophageal varices, a silent ulcer and gastritis. I do not see how I can make a more logical explanation. To the best of my knowledge I have never seen ascites associated with a single hemorrhage from ulcer.

DR PITTMAN. We did not believe that it was possible for anyone to make a definite diagnosis on this woman, or at least, I did not believe that it was. She was moribund when she came in, and her daughter added little to the history. I thought, as reported on the record, that a malignant neoplasm was likelier than cirrhosis. The resident bet on cirrhosis with esophageal varices, because he had been impressed with the fact that liver disease does occur in long-standing arthritis.

DR MARIAN W. ROPES. The impression that cirrhosis commonly occurs in arthritis is due to the fact that we recently had several patients with this combination. In general, the only evidence that we have comprises minimal changes in liver function in a fairly large number of cases.

CLINICAL DIAGNOSES

Cancer of stomach
Cirrhosis of liver, with esophageal varices?
Rheumatoid arthritis, chronic

DR JONES'S DIAGNOSES

Carcinoma of stomach, secondary to polyp
Rheumatoid arthritis, chronic

ANATOMICAL DIAGNOSES

Portal cirrhosis of liver, with ruptured esophageal and gastric varices
Hemorrhage into gastrointestinal tract
Ascites
Rheumatoid arthritis, chronic

PATHOLOGICAL DISCUSSION

DR CASTLEMAN The autopsy showed an atrophic, cirrhotic liver, weighing 1000 gm. Microscopically it appeared just like the ordinary garden variety of portal cirrhosis. The process was healed, showing a lot of scarring and surrounding areas of regeneration. The spleen was enlarged, weighing 500 gm. She was a small woman, and probably the reason the spleen could not be felt was that there was 2000 cc of ascitic fluid. The lower three fourths of the esophagus and the first 3 or 4 cm of the stomach

contained huge distended veins, and although we could not find the exact bleeding point at the time of autopsy, which is often the rule because it usually seals over, there is no doubt that a ruptured varix was the source of the hemorrhage. The entire gastrointestinal tract was filled with blood.

DR JONES Which were larger, the esophageal or the gastric veins? The reason I ask is that I am sure that the x-ray examination four months before entry was not a careful one.

DR PITTMAN I do not believe that she ever had a careful x-ray examination. She was terribly bent over and crippled by the arthritis, and it is dubious that she could have had an adequate gastrointestinal x-ray study.

DR JONES We have seen bleeding from gastric varices on few occasions, sometimes due to portal hypertension associated with cirrhosis of the liver or disease of the spleen and splenic vein.

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POSTGRADUATE TRAINING OF MEDICAL OFFICERS

DURING 1944, questionnaires requesting information concerning their wishes regarding future medical training were mailed to the approximately 60,000 medical officers on duty with the Army, Navy, Public Health Service and Veterans' Administration. The information contained in the questionnaires returned by 21,029 medical officers is analyzed in the final report,* and the resulting figures present a challenge to all organizations that are considering programs designed to meet the educational requirements of the discharged medical officer. Further-

more, the analysis indicates that certification by a specialty board is the ultimate goal of the young physician — a trend that may materially alter methods for the practice of medicine in the immediate future.

The percentages of officers expressing a desire for long (six or more months) and short (less than six months) courses of instruction were 59.6 and 21.7, respectively, the remainder stating that they did not want any future training.

The ten most popular subjects for the long courses were, in order of frequency, as follows: surgery, internal medicine, obstetrics and gynecology, general review, psychiatry and neurology, pediatrics, orthopedic surgery, ophthalmology, radiology and otolaryngology. The corresponding topics for the short courses were as follows: internal medicine, surgery, general review, obstetrics and gynecology, pediatrics, otolaryngology, ophthalmology, psychiatry and neurology, radiology and orthopedic surgery.

Sixty-three per cent of the group stated that they wished to become certified specialists, and nearly 16 per cent had already been certified by one of the specialty boards. This is all the more surprising when it is learned that nearly 40 per cent of these medical officers had entered military service from private practice.

If one applies the percentages of those desiring long and short courses of instruction to the approximately 60,000 medical officers on active duty, one obtains the figures of 35,800 and 13,000, respectively. Such numbers are sure to tax, if not overwhelm, any scheme of postgraduate instruction that might be devised. It is possible that the eventual figures will not be so large and that the times of discharge will be so staggered that the full impact will be avoided, but in any case, all agencies concerned with supplying these educational facilities — medical schools, hospitals and national, state and local medical societies — should be actively devising methods to meet the demand. This is particularly imperative because of the shortage of medical-school graduates that is bound to occur within the next few years, owing to the shortsighted regulations regarding deferment.

The fact that nearly 80 per cent of this group of relatively young physicians are either certified or

*Lueuth, H. C. Postgraduate wishes of medical officers. Final report on 21,029 questionnaires. *JAMA* 127:759-770, 1945.

desire to become certified by one of the specialty boards is difficult to evaluate. Certainly the practice of medicine has not reached the point — and probably never will — where 20 per cent of the licensed physicians can care for the ordinary aches and pains of the population, indeed, a reverse of the figures appears to be more accurate. Undoubtedly the need for certified specialists is constantly increasing as the science of medicine advances, but the general practitioner must still serve, particularly in small cities, towns and rural districts, unless, perhaps, medical practice is to be radically altered.

PENICILLIN AND SYPHILIS A WARNING

PENICILLIN has been used in the treatment of syphilis in various stages and has been found effective in clearing up the manifestations of the disease. Stokes,¹ in discussing the treatment of late syphilis with penicillin, states that it produces symptomatic and serologic transformations that are equal if not superior to those obtained by long and arduous procedures with arsenic and heavy metals. Moore² reviews the history of chemotherapy and concludes, "The rapid and safe cure of early syphilis is just around the corner." He qualifies this statement, however, as follows: "How best to use it [penicillin], alone or in combination with other forms of treatment, is as yet undetermined but is under organized nation-wide, governmentally sponsored study, from which definite results may be expected rapidly to emerge." This new form of therapy has spurred investigation into other rapid methods of treatment, employing large and frequent doses of agents heretofore used. Although the reports of results by all these methods are distinctly encouraging it should be remembered that the determination of the ultimate cure of syphilis is a long-range process measured in years rather than in months. The ability of the *Treponema pallidum* to remain dormant for many years and even affect the second generation many years after birth has been demonstrated all too frequently in the past.

With these tragedies in mind it is well to mix a word of caution with enthusiasm for a new method of treatment until the end-results are definitely known. It is therefore of special importance that all

patients treated for syphilis in this interim of determining the proper and infallible method, if such can be found, should be followed up serologically and physically with great care over a period of years. Every returning veteran who has been given penicillin for syphilis should therefore be re-examined from time to time to prevent, so far as possible, the late ravages of the disease in himself and his family.

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MASSACHUSETTS MEDICAL SOCIETY

DEATHS

GREENWAY — Major Thomas H. Greenway, A U S, formerly of Three Rivers, died June 23 at the Cushing General Hospital, Framingham. He was in his forty-fifth year.

Dr Greenway received his degree from Tufts College Medical School in 1927 and for a time maintained offices in both Three Rivers and Palmer. He served for a number of years as a member of the board of health and as associate medical examiner for this district. Shortly after entering the Army, in June, 1942, he was sent to the South Pacific as medical officer with an amphibious engineers' unit. At Lae he was named for conspicuous heroism when, after being buried under the debris of a falling building, he dug himself out and continued to direct under enemy fire the care of the wounded. After being hospitalized in Australia for a severe case of malaria, he returned to active duty and, while participating in landing operations in an island invasion, received an injury to his back, which resulted in his return to this country for treatment. He was a member of the staff of the Wing Memorial Hospital, Palmer.

His parents, his widow, two daughters, a son and four sisters survive.

PATTERSON — Alice M. Patterson, M D, of Marblehead, died June 20. She was in her seventy-sixth year.

Dr Patterson received her degree from Tufts College Medical School in 1904.

TRUESDALE — Philemon E. Truesdale, M D, of Fall River, died June 12. He was in his seventy-first year.

Dr Truesdale received his degree from Harvard Medical School in 1898. He joined the medical corps of the United States Army in 1917 and sailed for France with the rank of captain in the Yale Mobile Hospital Unit. In October, 1918, he was promoted to the rank of major. On his return to the United States he was assigned as director of surgery at Camp Devens and honorably discharged on March 15, 1919. He was president of the Bristol South District Medical Society from 1927 to 1928 and a councilor at the time of his death. He was a member of the House of Delegates of the American Medical Association in 1929. In that same year he was awarded a gold medal in the Scientific Exhibit of that Association for an exhibit showing experimental demonstration of the mechanism of transportation of abdominal viscera following rupture of the diaphragm. He was director of the Truesdale Hospital, which he had founded. He was a member of the founders' group of the American Board of Surgery and a member of the American Surgical Association, New England Surgical Society and the American Association for Thoracic Surgery. He was a fellow of the American College of Surgeons.

His widow, three sons and four daughters survive.

MEDICOLEGAL ABSTRACT

Right of Compensation Proof of performance of Christian Science practitioner's services In a recent Vermont case a Christian Science practitioner encountered some difficulty in proving that he had actually performed services for which the plaintiff was claiming compensation. The practitioner was not himself the plaintiff, the suit being brought by the person to whom he had assigned his claim. It appeared that it is a violation of the rules of the Church for a Christian Science practitioner to bring a suit at law to recover for treatments given to a patient.

To the Court it seemed the jury could have found that "the nature of the treatments with which we are here concerned is such that the defendant could have no way of knowing whether they were in fact given him, except what Haskins [the practitioner] stated about that matter. The treatments can be given to a patient when absent as well as when present." The Court stated:

Haskins is the only one who knows whether he did in fact give the treatments in question. Neither the defendant nor anyone else can have any knowledge of this matter except what Haskins states about it. While he testified that he gave the treatments in accordance with the tenets of his church, yet, when asked to explain just what he did in giving such treatment, his answers were evasive, several not responsive and several were contradictory. Repeated efforts by the defendant's counsel failed to get any clear cut or definite statement as to just what he did in the giving of such treatment except that such treatment was some form of prayer. Neither could it be learned from him how long such treatments took or just when he claimed he gave them. Such uncorroborated testimony is not of a character to compel a verdict for the plaintiff."

The Court's opinion makes it perfectly clear that the decision is not to be construed as denying the right of a Christian Science practitioner to recover for treatments actually given. It does not go so far even as holding that the evidence required the jury to find against the practitioner, but goes only so far as holding that the jury was reasonable in doing so. The opinion, however, may possibly be interpreted as holding that a jury is always free to disbelieve the testimony of the practitioner that he gave the treatments unless it is corroborated by the testimony of someone else to the same effect. And if this is the correct interpretation, the claim of a practitioner for compensation for treatments given when neither the patient nor anyone else was present is a somewhat precarious claim — (*Kennedy v Williams*, 114 Vt 54, 39 Atl 2nd 193 [1944])

CORRESPONDENCE

DIETS

To the Editor It is 11 p.m., my four young ones are in bed, and my husband at the hospital, so I have finally had a minute to pick up the *Journal*, which came this noon, and, praises be, I finally have an answer for the people who dis-

prove of the way we feed our children. My husband has said ever since we had the first that accepted child feeding is full of "pedigreed bunk," but try to convince a mother or a neighbor who thinks that you are not feeding your babies "scientifically"! I feel like framing your editorial "The Case against Fried Foods." It was only today that I thought of writing a medical magazine to ask, What is the difference between fish fried in fat and fish broiled with fat brushed on it? Our children have eaten from the family table from a very early age, to the horror of most beholders and they are a fine healthy crew. However, since many well meaning interlopers prefer quoted authority to the evidence of their eyes, I am delighted to have something to quote. Thank you for easing the life of a harassed and busy mother. Now if I could only convince my mother that a small piece of home-made fruit cake is no worse for a child than, say, a slice of raisin bread, a few nuts and a piece of plain cake, eaten separately at the same meal, I would be all set.

ALISON BARSTOW MATHERS
(Mrs. Frank P. Mathews)

Vashon, Washington

* * *

The *Journal* always welcomes any criticism of its editorial policies, particularly if the criticism is couched in terms of praise. We, too, have our vanities. Liberal as our policies are, however, even to the point of radicalism, we would not have our readers believe that we have entirely abandoned the idea of certain diets being suitable for children, and others, in a mild sense, for their parents. As Boswell said, "Claret is the liquor for boys, port for men, but he who aspires to be a hero must drink brandy." — Ed

BOOK REVIEWS

Trichinosis By Sylvester E. Gould, M.D., D.Sc. 8°, cloth 356 pp., with 128 illustrations. Springfield, Illinois: Charles C. Thomas, 1945. \$5.00.

This book is essentially a digest of the important publications on trichinosis from its earliest history to, and including 1943. The subject matter is well organized, and the illustrations, most of which are photomicrographs, are excellent. Dr. Gould has produced the best monograph on trichinosis since that of Stäubli written in 1909.

Surgery of the Hand By Sterling Bunnell, M.D. 4°, cloth 734 pp., with 597 illustrations. Philadelphia: J. B. Lippincott Company, 1944. \$12.00.

"Trauma involves all types of tissue, irrespective of the artificial divisions of our specialties. The surgeon must face the situation and equip himself to handle any and all of the tissues in a limb." This quotation from the preface underlies the high aim that the author has set himself in writing this excellent book, and it should be said that he has achieved his objective in a remarkable manner.

The book is divided into four parts. The first deals interestingly with the phylogeny and comparative anatomy of the hand and then proceeds to a discussion of the normal hand from the point of view of the skin, movements, mechanics of muscle and tendon, surgical anatomy, ossification and skeletal maturation. The second is a profitable account of the reconstruction of the hand, its examination, principles and operative technique as applied to problems of the skin and flexion contractures, bones, joints, nerves, tendons and muscles and concludes with a chapter on the arm in its relation to the hand. The third takes up in detail the question of injuries, infections and concludes with a vital discussion of the hand in industry. Finally, the fourth presents a succinct account of congenital deformities, vasomotor and trophic conditions and tumors of the hand.

This excellent book is particularly enhanced in its usefulness by the introduction of nearly six hundred beautiful illustrations. The references are timely and adequate, and one finds a good index. There is no doubt that every library will have this splendid book on its shelf, but it is urged that student interns and surgeons purchase their own copies.

(Notices on page xvii)

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ANESTHESIA BY COMBINED INTRAVENOUS PENTOTHAL SODIUM AND LOCAL NERVE BLOCK*

JAMES C McCANN, M D, Ph D (SURG)†

WORCESTER, MASSACHUSETTS

ANESTHESIA and anesthetic methods have properly concerned the surgical profession as its technical procedures have been perfected. Without adequate anesthesia, an otherwise ideal technical procedure is a matter of trial to the surgeon and a physiologic burden to the patient. Yet the acceptance of anesthetic methods by the surgeon for application to his patients reveals a curious picture of diversity and sectionalism. As far back as 1922 an editorial in the *Lancet*¹ posed this unanswered query "It would be interesting to ascertain why it is that in England and America general anesthesia has been developed at the expense of local, while on the Continent the reverse process has taken place." Gorth,² in reporting a clinical trip abroad for the study of anesthetic methods, as late as 1938 made the following interesting observations:

Anesthesia on the Continent has lagged behind anesthesia in the United States. Recently, however, a large number of Continental clinics are using intravenous anesthesia extensively not only for minor and short operations, but for all kinds of surgery. However, it may be that they are really setting the pace for us rather than going off at a tangent as it now appears. With modifications, then, such as the use of Pentothal during the induction of the splanchnic block, it seems we might perhaps do well to follow Finsterer in our handling of upper-abdominal surgery.

In America there is now a distinct sectionalism in the use of intravenous Pentothal Sodium for major surgical procedures. Reports from some sections indicate marked enthusiasm for its employment for all types of surgical cases, of whatever magnitude. These reports seem at times to lack careful and forthright reporting of the dangers of this method of anesthesia when incautiously administered. On the other hand, probably more frequently in discussion than in writing, one encounters in other sections quite arbitrary and dog-

matic criticism of what is clearly becoming a valuable addition to the methods of anesthesia.

Having carried out short operations under intravenous Pentothal Sodium administered by the syringe method for several years, I and members of the Anesthesia Department at St. Vincent Hospital developed an interest in the use of Pentothal Sodium for major surgical procedures. The approach was based on a systematic attempt to combine intravenous Pentothal Sodium and regional nerve block in a complementary fashion, whereby each would compensate for the inadequacies and undesirable features of the other. After a year of work with this method, it has been brought to such a satisfactory state that in all age groups and in all general surgical cases, except the few enumerated below, it has become entirely the anesthesia of choice for major as well as minor surgical operations. The exceptions are operations in children under seven or eight years of age, because of the small caliber of the veins, operations about the neck, in the absence of intratracheal intubation, because of the too easy stimulation of reflex laryngospasm, operations on patients over sixty years of age who are to undergo a prolonged operative procedure, because of the unsatisfactory metabolic destruction of large doses of the drug and the danger of pulmonary edema from prolonged depression, operations on patients with vomiting, asthma or abdominal distention.

The degree to which combined intravenous Pentothal Sodium and local nerve block has become in our hands the anesthetic of choice for general surgery (excluding its orthopedic branch) is indicated by the selection of anesthesia for the last 784 cases operated on by me during the past year. Local anesthesia was used in 95 cases, spinal anesthesia in 96, inhalation anesthesia (nitrous oxide or cyclopropane or ether) in 80, Pentothal Sodium by syringe in 124 and continuous-drip Pentothal Sodium with local nerve block in 389 cases. Thus, intravenous Pentothal Sodium was

*Read by title at the annual meeting of the New England Surgical Society, Boston, September 20, 1944.

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the major anesthetic agent in 64 per cent of approximately 800 surgical cases of all types. The other agents were each used in about 10 per cent of the cases.

It is becoming generally recognized that intravenous Pentothal Sodium as the sole anesthetic agent does not provide adequate muscular relaxation in an acceptably high percentage of cases, unless used in an excessive quantity that encroaches on the danger zone of respiratory depression. This has led to a search for satisfactory combinations with other methods to provide a satisfactory and safe anesthesia. It is well recognized that supplemental administration of extremely small amounts of cyclopropane or ether quickly and completely takes up the deficiencies of Pentothal Sodium with respect to relaxation. Many surgeons have reported the supplemental use of nitrous oxide and oxygen with this drug, but in our hands it was not found to afford additional help at all comparable with the results procured by the complementary use of regional nerve block. In the few cases in which this combination failed to provide sufficient relaxation of the accessory muscles of respiration to permit easy closure of the peritoneum, nitrous oxide and oxygen did not produce an iota more of relaxation. The deficiency was quickly taken up by a small amount of cyclopropane or nitrous oxide and ether. This situation arose in only 3 or 4 per cent of the cases. No supplemental anesthesia was needed in the rest. Interrupted oxygen administration was carried out, however, when there was the least suggestion of cyanosis, in all cases of anemia, in all prolonged cases and in elderly patients who undoubtedly had some arteriosclerosis or myocardial changes.

Recent reports on the use of curare, a short-acting drug that paralyzes the myoneural junction of skeletal muscles, to produce relaxation is of interest, although its total systemic action indicates caution in its use until it has been thoroughly investigated.

In this series, Pentothal Sodium was administered in a 1 per cent solution by the continuous-drip method, which has been well described in the literature. In the infrequent cases in which the veins were so small as to cause an unsatisfactory rate of flow, a 2 per cent solution was used. After induction, the drug was administered during the period of maintenance in repeated and grouped subminimal fractions of either 5-cc or 10-cc amounts, depending on the rate of metabolic destruction of the drug in the given case. Between each subminimal fraction there was a wait of one minute to observe its effect on the respiratory center. The drug was given from the usual intravenous-infusion apparatus, with the drops regulated through a Murphy drip to about 250 drops per minute for induction and to about 130 to 140 per minute for maintenance. A companion infusion

apparatus provided for continuous administration of saline or glucose solution during the intervals between the groups of Pentothal Sodium fractions, and for the instantaneous administration of plasma or blood without disturbing the patient during the operation. The intervals between fractions were five to fifteen minutes. Having observed the syringe technic for several years, we adopted the above method as the simplest, most dependable and most flexible way of administering Pentothal Sodium.

Local anesthesia — by 1 per cent novocain — was used to take up the deficiencies of the Pentothal Sodium. In the rare cases in which skin sensibility was of so high an order that it was not readily obliterated with the usual quantities of Pentothal Sodium, quick infiltration of the line of incision with novocain permitted this barrier to be easily passed. Relaxation of the rectus muscle comparable to that of spinal anesthesia was procured by direct block of the intercostal nerves in the rectus sheath. Patterns of blocking the sympathetic or intercostal nerves according to the type of operation were mapped out from the background of general experience with regional anesthesia.

In major abdominal operations, Pentothal Sodium alone was capable of controlling all reflexes arising from ordinary manipulations within the peritoneal cavity. Deep reflexes, however, which are elicited by traction on the viscera or their mesenteries, and whose control would have required deep planes of Pentothal Sodium anesthesia, were eliminated by blocking the sympathetic pathways with novocain. This was accomplished in the upper abdomen by anterior splanchnic block, in operations on the bowel by mesenteric block and in pelvic operations by block of the ganglions and sympathetic nerves involved.

This complementary use of the two agents provided a completely satisfactory anesthesia, comparable in all respects, and superior in many, to spinal or deep general anesthesia. It was accomplished with the administration of only moderate doses of Pentothal Sodium. If the two methods are effectively combined, the result provides a speedy, safe type of anesthesia, with an induction and recovery experience strikingly freer of unpleasant and uncomfortable episodes than is the case with the other principal anesthetic methods. Nausea and vomiting are infrequent, postoperative catheterization of male patients is rarely necessary, and in cases of herniorrhaphy has practically disappeared, postoperative headache does not occur, the administration of parenteral fluid, except as required by the technical exigencies of the operation, is reduced almost to the vanishing point, and early ambulation is favored.

Particular consideration should be given to the question of anterior splanchnic block. The method of choice for upper abdominal operations on the Continent, it has found but limited favor in America.

Finsterer and Thorek³ and de Takats⁴ in particular have used it in America. Combined with skillfully administered Pentothal Sodium anesthesia and rectus block, it constitutes an ideal anesthetic method for all operations on the stomach, spleen, gall bladder and ducts. The patient sleeps throughout the operation, there is complete flaccid paralysis of the rectus muscles, there is no reflex stimulation of the respiratory center from traction on the mesentery of the stomach or gall bladder, there is free delivery of the organs up into the incision, there is controllable respiratory quietude, there is never retching, nausea or vomiting, there is very rarely any drop in blood pressure, the pulse does not usually rise, and rarely passes 100, the patient can be maintained in an extremely light plane of Pentothal Sodium anesthesia, there is comfortable and not too delayed recovery from the anesthesia, and instantaneous operative support by the administration of plasma or blood is available as well as continuous saline or glucose infusion, without other disturbing manipulations. Little more can be asked to classify an anesthesia as nearly ideal.

In 1918, Kappis⁵ first published detailed reports of 200 cases operated on under posterior splanchnic anesthesia by the paravertebral approach. In the same year, Wendling⁶ suggested blind penetration of the unopened abdominal wall with a long needle at the level of the first lumbar vertebra to produce splanchnic anesthesia, but of course such a suggestion was never seriously considered. In 1919, Braun⁷ reported the use of anterior splanchnic block by way of the opened abdomen. Finsterer has been an ardent advocate and practitioner of the method, as have been many German surgeons. In 1926 he and Thorek³ reported 2373 cases collected from the literature and personal communications from several German surgeons without a single anesthetic fatality, they were unable to find a single death from this method up to 1936.

The use of splanchnic anesthesia in this series has controlled the strong reflex stimulation of the respiratory center from traction on the subdiaphragmatic mesenteries, the activation of which leads to a high rate of utilization of Pentothal Sodium. During anesthesia from this drug alone these deep powerful reflexes make surgery difficult as a result of extreme activation of the muscles of respiration, particularly the lateral abdominal muscle and the diaphragm. Large doses of Pentothal Sodium administered to suppress this forced breathing activity encroached on the zone of respiratory depression to such an extent that in a few cases transient apnea was encountered. Splanchnic anesthesia controls these undesirable restrictions on the use of Pentothal Sodium, and provides abdominal quietude, adequate relaxation of the accessory muscles involved in the stimulated breathing and minimal excursions of the diaphragm. These effects result in a reduction of about 1 gm in the

average total dosage of Pentothal Sodium required. This is illustrated by two series of cholecystectomies, each comprising 22 cases. In the first series, in which Pentothal Sodium and rectus block were used, the average dose of the drug was 2.19 gm, in the second series, in which splanchnic block was added, the average dose was 1.23 gm.

It will be appropriate to report a modified technic for anterior splanchnic block, based on a special splanchnic needle guide that I devised (Fig 1).

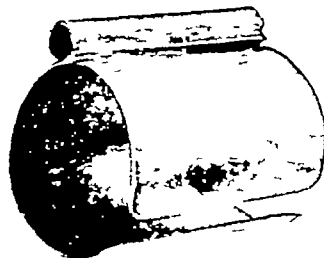


FIGURE 1 Splanchnic Needle Guide

The modification and the guide convert a moderately difficult technical procedure, particularly in the obese abdomen, into a relatively simple and safe procedure. With this modification the procedure was carried out with ease in a deep-chested, obese patient weighing 235 pounds. The purpose of anterior splanchnic block is to deposit an anesthetizing dose of novocain retroperitoneally at the level of the first and second lumbar vertebrae between the aorta and the inferior vena cava. This is an isthmus point or meeting place for all sympathetic nerves and plexuses deriving from the greater and lesser splanchnic nerves and the sympathetic trunks, which supply the stomach, duodenum, pancreas and transverse colon. In the usual technic the finger is pressed downward above the lesser curvature of the stomach and cephalad to the upper border of the pancreas as well as the celiac axis, until it encounters the body of the first lumbar vertebra. In so doing it carries the lesser omentum in the hilus region of the liver down under it, so that resistance and intervening vague fatty tissues confuse the certainty with which the tip of the finger contacts the vertebra and keeps free from underlying structures. The aorta is identified on the right side of the fingertip, and by pressing the aorta to the patient's left and pressing firmly on the vertebral body, the aorta is safely separated from the inferior vena cava. The novocain needle is then inserted directly over the tip of the finger until it distinctly contacts the body of the first lumbar vertebra, when the novocain is injected. The technic may be decidedly difficult in an extremely or even a moderately obese patient. There is a distinctly blind aspect to this technic.

My modified technic makes the procedure certain, safe, easy and exact. With the patient satisfactorily

anesthetized with Pentothal Sodium, two broad-bladed retractors are placed under the left and the adjacent portion of the right lobe of the liver, retracting them upward. A pack is placed along the lesser curvature and over the anterior surface of the stomach so that the left hand can retract it downward, tensing the lesser omentum, particularly where it enters the hilus of the liver. Lateral pressure to the patient's left by the index finger over the corner of the pack carries the fundus of the stomach outward and improves exposure. About in the midline the caudate lobe of the liver is nearly always identified behind the lesser omentum, where the omentum passes between the left lobe of the liver and the caudate lobe. The caudate lobe has a purplish-brown appearance behind the thin screen of the omentum. With the omentum still tensed by downward traction of the left hand, a vertical rent is established in this avascular lesser omentum by an instrument, directly over the tip of the caudate lobe. This permits the caudate lobe to move forward into the rent so that its tip presents in front of the omentum. Usually this area is free of fat and completely avascular, although an occasional vessel may traverse the area. In extremely thin persons nothing is gained by opening the omentum. The tip of the middle finger of the left hand is then advanced cautiously through the rent into the lesser omental bursa, until it comes into direct contact with the body of the first lumbar vertebra. There are now no obscuring membranes between the finger tip and the bone. The pulsating aorta is identified above the celiac artery and the upper border of the pancreas.

The finger and hand are then withdrawn. The splanchnic needle guide is fitted over the second and third phalanges of the middle finger of the left hand. The left hand is again placed in its previous position of retraction over the stomach, again advancing the middle finger, this time bearing the splanchnic needle guide, under the caudate lobe and into the lesser omental cavity, until it again contacts the first lumbar vertebra as a distinct bony structure with no intervening membranes. Pressure firmly applied to the patient's left against the pulsing aorta and downward against the bone safely separates the aorta from the inferior vena cava. A strong 15-cm 18-gauge needle, attached

to a novocain syringe, is inserted in the proximal opening of the small needle guide, through which it is easily and accurately advanced until it impinges abruptly and definitely on the first lumbar vertebra, directly over the tip of the nail of the middle finger, and separated from it by a few millimeters. If desired, the splanchnic guide may be slightly rotated so that the needle can advance a fraction to the right or the left of the middle of the finger tip, according to the dictates of the underlying anatomy of the aorta.

When firm contact by the needle point against the body of the vertebra has been established, 20 cc of a 0.5 per cent novocain solution is injected. During a long operation 10 cc may be repeated hourly. Almost immediately respiratory quietude and relaxation pervade the whole subdiaphragmatic region, with complete obliteration of the disturbing reflex stimulation of respiration previously evoked by traction on the upper abdominal viscera or their mesenteries.

SUMMARY

A brief preliminary report is presented concerning a satisfactory experience during the past year in using intravenous Pentothal Sodium anesthesia with regional nerve block for major surgical procedures in a complementary fashion.

A modified technic for anterior splanchnic block anesthesia, based on the use of a needle guide improvised for accurately carrying the splanchnic needle to assured and safe contact with the first lumbar vertebra, is presented.

Following rather extensive experience with this method, a search was made in the literature for the report of a device like the above-described splanchnic needle guide. Only one brief note was found. Burke⁸ used the same basic principle. He attached a flexible ring to the end of a long grooved director and used the director to guide the splanchnic needle.

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DEATH FROM SULFADIAZINE WITH AGRANULOCYTOSIS, JAUNDICE AND HEPATOSIS

Report of a Case

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LIEUTENANT COLONEL JAMES N PATTERSON, MC, AUS,
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THE occurrence of various types of toxic reactions to the sulfonamides is now common knowledge, and all have been fully described in the medical literature¹⁻⁵ in recent years. There have been reported a sufficient number of severe reactions producing death to make the medical profession fully conscious of this danger and of its obligations in this respect. Reactions from the newer compounds have been fewer than those from the older ones. Thus, those seen following the use of sulfathiazole are much less frequent than are those from sulfanilamide, and those resulting from sulfadiazine appear to be still fewer in number. Although agranulocytosis and focal necrosis of the liver have been seen as manifestations of toxicity due to sulfathiazole administration, we, who are not in a position to make a thorough search of the current literature, are not familiar with any report of agranulocytosis and liver damage following the use of sulfadiazine. Simon¹ in a comprehensive review of the pathologic lesions seen in both animals and man states that the most extensive and widespread types of focal necrosis of the liver are seen in deaths following sulfathiazole therapy, but does not mention similar lesions resulting from sulfadiazine. The following case of death after sulfadiazine administration is cited as one believed to have resulted from agranulocytosis and jaundice, in which there was a diffuse hepatitis of moderate degree and marked congestion and early central necrosis of the liver.

CASE REPORT

The patient, a 23-year-old man, had been ill with abdominal pain for 72 hours prior to admission to a regional station hospital of the Army Air Force in Florida. He had previously been in good health and could recall no previous illnesses of any account. He was closely questioned regarding any previous administration of the sulfonamide drugs and was positive that none had ever been given. The history was typical of acute appendicitis, with generalized abdominal pain that had persisted for 24 hours, followed by pain in the right lower quadrant for 48 hours. It was unaccompanied by nausea, vomiting, chills, fever or urinary complaints, and there had been no bowel movement for 3 days.

Examination of the abdomen on admission revealed it to be flat and without distention, muscle spasm or the presence of a mass. Localized tenderness was present in the right iliac fossa, but rectal examination revealed no tenderness or induration. The white-cell count was 10,250, the pulse 100, and the temperature 101.2°F. The policy in this hospital was not to subject any patient to operation for appendectomy if it was thought that perforation of the appendix had occurred but rather to treat such cases conservatively. This case, however, did not suggest perforation, and the patient was operated on under spinal anesthesia within a few hours of admission. When the peritoneum was opened through a McBurney incision, foul-smelling, cloudy fluid was encountered, from which a paracolon bacillus was cultured. The appendix was adherent to the cecum, the wall of which was markedly in-

durated. Inasmuch as attempted removal of the appendix would have been extremely difficult the operation was concluded by placing 10 gm of sulfanilamide in the peritoneal cavity in the region of the appendix and closing the wound in layers around a cigarette drain.

Postoperative treatment consisted of constant Wangensteen suction supportive therapy with adequate fluid intake intravenously, morphine, nothing by mouth and 5 gm of sodium sulfadiazine administered in two doses daily by the intravenous route (Fig 1). The course was somewhat stormy for 9 days, during which time the temperature fluctuated in the neighborhood of 102°F and the pulse around 100 per minute. Considerable distention developed in spite of the continuous gastric suction and on the 8th postoperative day this had reached such proportions that it was thought advisable to pass a Miller-Abbott tube. This was successfully passed into the duodenum, whence it rapidly traveled to the lower ileum and decompressed the abdomen completely within 12 hours. The temperature was normal on the 9th day, intestinal suction being discontinued on the 12th day. Intravenous sulfadiazine was discontinued on the 11th postoperative day, and thereafter was given in 2-gm daily doses by mouth until the 18th day.

During this entire interval the blood chemical findings and cell counts were satisfactory, and although the wound continued to discharge a moderate amount of pus, the patient appeared to be making a satisfactory recovery after the 12th day.

On the 16th postoperative day, the temperature reached 100°F, and increased daily so that by the 21st day it had reached 104°. The distention did not recur, and repeated examinations of the abdomen and rectum revealed no evidence of a recurrence of abscess formation. Fluoroscopic and x-ray studies of the diaphragm and chest were normal. Two days after the onset of this fever the daily 2-gm dose of sulfadiazine was discontinued in the belief that this might have accounted for the febrile reaction, but the temperature continued to rise for 4 more days. The white-cell count which was 9000 when the drug was discontinued, dropped to 4000 on the following day, but rose to 5900 on the 21st day. The possibility of pyelphlebitis and multiple liver abscesses as a cause for the fever was entertained, but there was no evidence of icterus or ascites of even mild degree. On the 22nd day of the illness, it was believed that there was some increased induration in the region of the wound that might possibly account for the recurrence of fever, and a second operation was therefore undertaken.

Under intravenous Pentothal Sodium anesthesia the original wound was explored with the finger. Although it was unhealthy in appearance, no abscess pockets were encountered, and the operation was concluded in 10 minutes. While the patient was on the operating table there again was considerable discussion by members of the staff concerning the cause of the fever. Pyelphlebitis with multiple liver abscesses was again considered. Several medical officers inspected the scleras in a good light for evidence of an early jaundice, but none was seen.

Within 2 hours after the operation several dramatic incidents occurred. First, the patient developed cyanosis, which was rapidly and successfully treated with oxygen and intravenous caffeine sodium benzoate. During this time he was receiving 2.5 gm of sodium sulfadiazine intravenously. Within 1 hour marked jaundice suddenly developed, and blood studies revealed an icteric index of 106 (van den Bergh, 38 mg per 100 cc.), and the startling fact that the white-cell count had dropped to 450. Blood smears at that time revealed a total absence of granulocytes. These untoward developments were accompanied by a rise in temperature to 106°F and an increase in the pulse to 130.

For the next 5 days, the condition of the patient was critical, with the temperature fluctuating between 104° and 106°F and the pulse between 130 and 160. The jaundice increased,

the icteric index reaching 177 on the 3rd postoperative day. Although the serum protein level was above 6 gm per 100 cc, the albumin-globulin ratio dropped to 1:1. All the other blood findings, including the nonprotein nitrogen, blood phosphatase, chloride, hemoglobin and red-cell count, remained within normal limits. General supportive measures were undertaken, including the adequate administration of fluids, continuous oxygen and transfusion of 1000 cc of fresh compatible citrated blood daily. These procedures were of no avail, although the white-cell count did rise to 2450 and 2000 on the 3rd and 4th postoperative days. The smears, however, continued to show an absence of granulocytes in the blood, and the patient expired on the 5th day after the second operation, 26 days after admission.

Autopsy. Autopsy was started within 1 hour after death. The body showed evidence of considerable weight loss. The

The lower edge of the liver was 1 fingerbreadth below the right costal margin, the left lobe extending to the left anterior axillary line. The common bile duct and the hepatic duct and its large branches were opened upward from the ampulla of Vater, but no obstruction or stone was noted. The cystic duct showed no abnormalities. The wall of the gall bladder was not thickened and contained no stones. On section of the liver the edges everted markedly. The liver was reddish brown and on close inspection had a nutmeg appearance. The entire liver was sectioned into thin slices and presented the same picture throughout. The consistence of the organ was not changed to any appreciable extent.

The spleen was dark reddish blue and approximately three times its normal size. It was firm and retained its shape on removal from the body. The mucosa of the cecum was reddened, granular and swollen. The kidneys were swollen and

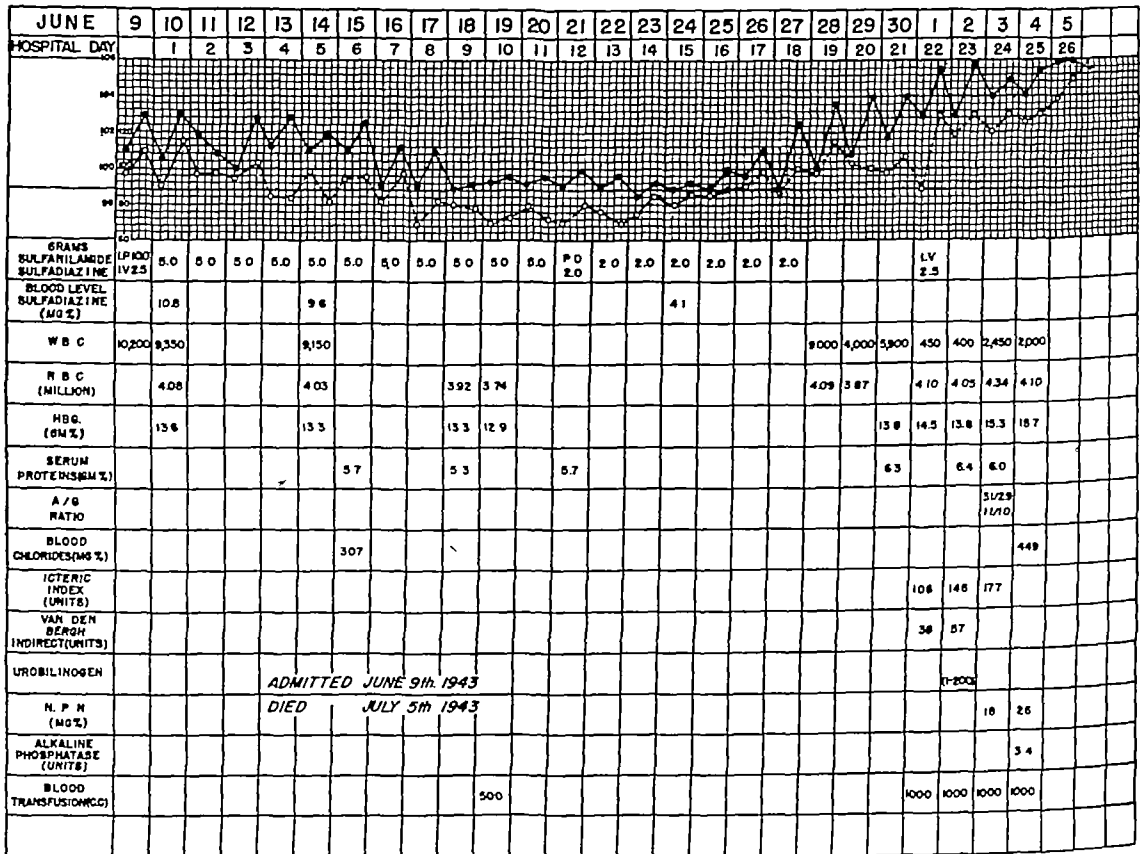


FIGURE 1

skin and conjunctivas were markedly icteric. Two cigarette drains were present in the recent McBurney's incision, along which was noted a small amount of foul-smelling, purulent-looking material. The greater omentum was pulled to the right and was held by thick fibrinous adhesions to the peritoneal lining of the right lower quadrant of the abdomen, thus walling off this area. The peritoneal cavity was otherwise unaffected except for approximately 5 cc of purulent-looking material walled off by thick fibrinous adhesions in the rectovesical space. The distal half of the appendix had been eaten away, and the wall of the stump was slightly thickened, and its serosa granular and reddened. The small tributaries of the superior mesenteric vein draining the terminal ileum, cecum and appendix were cross-sectioned approximately every centimeter of their distance and found to be patent, as were the arteries. The superior mesenteric and portal veins were opened throughout their length, but no thrombi or break in the intimal lining was observed. The regional lymph nodes were markedly enlarged, grayish yellow and fairly firm in consistence.

The edges everted on section. The cortex of each kidney was pasty yellow and was moderately widened. The medulla were injected. The capsules stripped with ease, leaving smooth, even surfaces. The suprarenal glands were of normal size but were slightly softer than normal.

The lungs showed no abnormalities other than for congestion and edema in the most dependent portions. The pleural cavities were free of adhesions. The pericardial cavity contained approximately 50 cc of bile-stained watery fluid. The pericardial lining was smooth and glistening throughout. The heart was flabby and did not retain its shape on removal from the body, the musculature being brownish red and soft. The coronary vessels were patent throughout, and the valves were not thickened. The intima of the first part of the aorta contained an occasional atheromatous plaque. The lining of the aorta had a yellowish tint, as did many other tissues throughout the body.

The bone marrow of the sternum and ribs was hypoplastic. Smears from sternal bone marrow showed a hyperplasia of immature myeloid elements with an apparent arrest of maturation.

tion at the myeloblastic level. Most of the cells appeared to be myeloblasts, containing from two to three nucleoli.*

Microscopical study of the tissue revealed less damage to the liver cells than had been expected from the deep jaundice. The central veins were engorged, with resulting atrophy and early focal necrosis of the adjacent liver cells. Fat stains revealed focal areas of fatty degeneration of the liver cells, which were more marked in the central areas. The remainder of the liver cells showed swelling, increased granularity and bile retention, but otherwise they were fairly well preserved. Study of many sections failed to reveal any evidence of obstructive dilatation of the intrahepatic bile ducts, which substantiated the autopsy finding of no obstruction of the large bile ducts. There was no histologic evidence of previous liver damage (this is often present in persons showing liver disease from sulfonamide drugs).

The appendix showed a subserosal zone of necrosis with bacterial colonization and with practically no cellular reaction. The reaction of the mesentery to the peritonitis was practically exclusively plasmocytic and lymphocytic, with an interspersed occasional macrophage and histiocyte. If only sections showing the reaction to the peritonitis had been seen, one would of necessity have considered seriously the rare entity of aleukemic plasma-cell leukemia.

Microscopical examination of the spleen revealed marked depletion of nucleated elements of both follicles and pulp. The kidneys showed normal glomeruli and cloudy swelling of the tubules. Many bile casts and an occasional hemoglobin cast were found.

A blood culture taken at the time of the post-mortem examination and grown on tryptose phosphate broth and heart-infusion broth showed a gram-positive rod, a gram-negative rod and a gram-positive coccus. This finding had little significance, since blood cultures taken a few days after the second operation and planted on the same mediums were still sterile after 21 days of incubation.

The points to be stressed in the progress of this patient are as follows. Up to the sixteenth post-operative day he was apparently making a satisfactory recovery from incision and drainage of a local peritonitis due to perforation of the appendix. Fever then recurred to an increasing degree daily, and four days after sulfadiazine therapy was discontinued the fever continued to rise, reaching a maximum of 104°F. Following the second operation a short period of anoxia occurred during the administration of 2.5 gm of sodium sulfadiazine intravenously. Sudden and rapid onset of jaundice,

*All these findings were confirmed by Dr Roy R. Kracke of Emory University.

accompanied by a marked leukopenia and agranulocytosis, occurred within one hour of administration of the sulfadiazine. Lastly, post-mortem examination showed no evidence of infection to account for the fatal termination, but did reveal a hyperplasia of immature myeloid elements, with an apparent arrest of maturation at the myeloblastic level in the bone marrow, and enlargement of the liver due to a diffuse hepatosis with early central focal necrosis. Histologic examination of the liver failed to give a completely satisfactory explanation for the intense jaundice.

In retrospect it is believed that the febrile reaction occurring from the sixteenth to the twenty-second postoperative day was a toxic reaction to sulfadiazine, the patient having received 71.5 gm of the drug up to the eighteenth day. It is further considered that the sudden development of jaundice and agranulocytosis after a further administration of 2.5 gm of sulfadiazine probably produced an exacerbation of the hypersensitiveness to sulfadiazine, with the resultant liver and bone-marrow changes that led to the fatal outcome.

SUMMARY

A fatal case following the administration of sulfadiazine and presumably due to toxic damage of the liver and bone marrow is described, and the post-mortem findings are discussed.

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TUMOR OF THE CAROTID BODY*

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— BOSTON

THERE is nothing new to be said in regard to tumors of the carotid body. The only excuse for presenting this subject to the surgical profession is a plea for a correct preoperative diagnosis. If this is made, it may well be possible to reduce the rather high mortality that has accompanied the surgical cure of this lesion.

The correct diagnosis should not be too difficult provided that one considers carotid-body tumor in the differential diagnosis. The only difficulty has been that this condition is not frequently encountered, and that therefore one fails to give it consideration.

The carotid body was first mentioned by von Haller¹ in 1743, and was described in detail in 1862 by Luschka.² It is a tiny organ about the size of a grain of rice situated at or near the bifurcation of each common carotid artery. It is supposed to reach full development at about the age of twenty, but in some cases it either does not exist or is so tiny that it is not found at autopsy. It is always closely attached to the wall of the carotid artery, but its exact location is not constant.

Embryologically the carotid body is a complex structure of somewhat disputed origin. By some it is supposed to arise from mesodermal tissue of the third branchial cleft and to be somewhat homologous to the medullary portion of the suprarenal gland. By others it is thought to have its origin in the sympathetic nervous system. Certainly it is well supplied with nerve fibers. It is intimately associated with the periarterial sympathetic fibers of the carotid artery, receives fibers from the glossopharyngeal nerve and the upper cervical sympathetic ganglion, and sometimes has a communicating branch with the vagus nerve.

Physiologically it is apparently of no great importance. There is little or no evidence in favor of including it among the glands of internal secretion. The facts that it is sometimes absent and that bilateral extirpation can be carried out without any subsequent symptoms suggest that its function, whatever it may be, is negligible. This being so, the only clinical interest in the carotid body is its pathology, and the only pathologic lesion is a tumor. It is said that the first recorded operation for tumor of the carotid body in America was performed by Middleton³ in 1895. The tumors in general maintain the same histologic characteristics as does the normal carotid body. Definite malignancy

as indicated by active mitosis is found in 50 per cent of the tumors, and all are potentially malignant. Distant metastasis has never been proved, but local recurrence has occurred in 20 per cent of the malignant cases.

The tumors are usually unilateral, but an occasional bilateral involvement has been reported. They manifest themselves as painless, slow-growing tumors situated in the superoanterior cervical triangle, pushing out from under the anterior border of the sternomastoid muscle. They are usually ovoid, firm but elastic and deep seated, and are never attached to the skin. They are extremely vascular. Sometimes a bruit or thrill is present, and often a transmitted pulsation from the carotid arteries is evident, but this is to be differentiated from the expansile pulsation of an aneurysm. Compression of the carotid artery below the tumor abolishes the bruit, thrill or pulsation and sometimes causes a diminution in its size. These tumors usually have some lateral mobility, but possess little or no vertical mobility because of their firm attachment to the carotid artery. This is an important diagnostic point.

Carotid-body tumor is a disease of middle age, the average age of patients being about forty-five years at the time of operation, but some of the tumors have been present from ten to fifteen years, with an average duration of five or six years.

When any other symptoms, aside from slow, painless growth, are present, they are usually caused by invasion or compression of other important regional structures, such as the vagus nerve, the sympathetic or recurrent laryngeal nerves or the pharynx or esophagus. Episodes of fainting, hoarseness, dyspnea, dysphagia, cough, tinnitus or headache have been reported, as has Horner's syndrome from pressure on the cervical sympathetic nerves.

The correct diagnosis of these tumors is rarely made preoperatively—in less than 10 per cent of the reported cases. This is undoubtedly due to the fact that the condition is so rare that its existence is not even considered by the examining physician. Only 20 cases of carotid-body tumor were to be found in the records of the Mayo Clinic in 1941, and somewhat over 200 in the entire medical literature.⁴ The most frequent incorrect diagnoses are tuberculous adenitis, branchial cyst, metastatic carcinoma, aberrant thyroid gland and aneurysm.

If the diagnosis of carotid-body tumor is considered at all, it should not be too difficult to arrive at the correct answer. The most important indica-

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tion of such a diagnosis is the presence of a slowly growing, painless, deep-seated tumor in the upper anterior neck, particularly if, as before mentioned, there is lateral mobility without vertical mobility, not to mention marked transmitted pulsation, and perhaps diminution in the size of tumor on cutting off the circulation by pressure on the common carotid artery.

The importance of establishing the correct diagnosis before operation is that steps can then be taken to reduce the dangers involved by the operative procedure. The chief danger is death from cerebral anemia or hemiplegia, should sacrifice of the carotid arteries be necessary at the time of excision.

It is generally accepted that surgical removal is the ideal treatment for tumors of the carotid body, particularly if this can be done without sacrifice of the carotid vessels. Some years ago, however, Bevan⁵ expressed the opinion that if the tumor proved to be inoperable without sacrifice of these vessels, the incision should be closed as would be done in any other exploration for inoperable disease, and the patient treated with radium or x-rays. Little is found in the literature, however, to indicate that these tumors can be treated successfully with radiation. There is also some doubt whether it would be possible to go no farther after exploring the tumor sufficiently to determine that the carotid vessels must be sacrificed. At such a point one might well be committed to a completion of the operation to control the bleeding from the extremely vascular tumor. A complete removal of the tumor is indicated even at the additional risk involved because of its malignant or potentially malignant nature.

In a series of 159 cases reviewed by Phelps, Case, and Snyder⁶ in 1937, the mortality rate was 24 per cent. In the series of 20 cases at the Mayo Clinic, reported by Harrington, Clagett and Dockerty⁴ in 1941, the mortality was 20 per cent, in the cases in which ligation of the carotid vessels was necessary it was 44 per cent. The average age of the patients who died following ligation was fifty-three, and that of those who survived it was thirty-one. This indicates an increasing risk with advancing age.

Because of this pronounced danger, particularly in old patients, it seems wise to give every possible preoperative preparation to the patient in whom a tumor of the carotid body is suspected. This preparation should consist of systematic compression of the common carotid artery against the transverse process of the sixth cervical vertebra. This pressure should be carried out for an increasing duration of time, and several times a day, over a period of several weeks if necessary, until the patient can tolerate complete compression of the vessel for long periods without experiencing faintness or loss of consciousness. Linton⁷ has developed a tourniquet

in the form of a rigid collar around the neck, pressure is exerted on the carotid artery by means of a pad activated by a screw. It is hoped by this procedure that the collateral circulation to the brain on the affected side can be improved.

There is some difference of opinion whether collateral circulation in this part of the body can be developed. Possibly in certain cases anatomic variation in the arterial circulation at the base of the brain may prove to be an unsurmountable barrier. Certainly if a patient has a so-called "carotid reflex," — namely, syncope caused by pressure on the carotid artery, — one should hesitate to divide the artery at operation unless the reflex can be abolished by some such development of collateral circulation as is suggested above.

There are of course other structures that may be injured during the operative removal of a carotid-body tumor. Some of these are the internal jugular vein, the vagus nerve, the recurrent laryngeal nerve, the hypoglossal nerve and the cervical sympathetic chain. With care and a proper technic, however, these injuries should be reduced to a minimum, and naturally they are not so serious as a hemiplegia.

The clinical case that brought this subject again to my attention is as follows:

CASE REPORT

M H, a 44-year-old, unmarried woman consulted me on January 18, 1944, because of an unsightly swelling in the right side of her neck. She had first noticed a small lump in this area in 1935. This had gradually increased in size. She had had no pain or discomfort, except for occasional attacks of headache.

Examination revealed a tumor in the upper neck, just anterior to the sternomastoid muscle, 7 cm. in diameter with the vertical dimension slightly longer than the horizontal. It was firm and nontender. There was a definite bruit and pulsation that seemed to come from surrounding vessels and not from the tumor itself. The latter was slightly movable in a lateral direction. There was a vertical scar 5 cm. long over the tumor where a surgeon had attempted several years previously to remove it, but had stopped the operation, explaining to the patient that he was not prepared for such a serious dissection as would be necessary for its removal. I believed that this tumor probably arose from aberrant thyroid tissue and advised operation.

Operation was done under a general anesthesia. Owing to the extreme vascularity of the tumor, every precaution was made to control all small blood vessels, and the dissection was carried out slowly and carefully through an ample incision. The tumor was eventually entirely exposed and seemed to arise from the bifurcation of the carotid artery. It could be dissected from the carotid, however, without damage to that vessel, and the wound was closed. The patient made a comfortable, uneventful recovery, being discharged from the hospital in 4 days. The pathologist reported a tumor of the carotid body, which had not been considered as a possible diagnosis.

SUMMARY

Tumors of the carotid body are rare, but should be considered in all slowly growing, painless tumors of the upper neck, and if considered, the correct diagnosis should be arrived at with reasonable accuracy. Their incidence is the same in both sexes. The majority of patients are between forty and sixty years of age.

These tumors are always either malignant or potentially so. They rarely recur, and almost never metastasize after complete surgical removal.

The operation is delicate and dangerous.

Ligation of the carotid vessels is necessary for complete removal in 50 per cent of the cases.

Preoperative preparation consists of systematic compression of the common carotid artery several times daily for gradually increasing periods until the patient can tolerate complete compression for long periods without syncope.

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MEDICAL PROGRESS

PSYCHIATRY: REHABILITATION

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CURRENT psychiatric literature continues to be composed, in great part, of papers dealing with the psychiatric casualties of war. It is now well established that the earlier treatment is begun the better are the chances for recovery. Of course the same principle applies, and always has applied, to the psychiatric illnesses of peacetime living. So much has been written, both in scientific journals and in the popular press, about war nerves, combat fatigue or psychoneurosis that not only the public but psychiatrists themselves may have lost a well balanced perspective on this subject. Also popular alarm has been augmented by the large number of inductees rejected as "not suited for military service" on the basis of a neuropsychiatric or personality disorder.

Although exact statistics are not available, it is reported^{1,2} fairly consistently that about 45 per cent of the medical discharges from the armed forces are for neuropsychiatric disability. Considering that the men receiving medical discharges to date constitute a small proportion of the grand total of those in service, the problem of the veteran who returns to civilian life with war nerves is not, and will not be, so appalling in extent as the alarmists portray. If qualities of human nature can be spoken of in the sense that human nature is at all responsible for them, it is a compliment to human psychobiologic integration that comparatively so few men become psychiatric casualties under the impact of the terrific conditions of combat.

There is, of course, the problem of rehabilitation for many men who develop nervous disorders during their time in service. Pratt³ states that as of September, 1944, more than 300,000 men had been discharged for psychiatric conditions. Important

considerations in this problem are insufficient facilities for treatment and the reluctance or refusal of numerous men to accept treatment. Even before the war, federal veterans' hospitals were overcrowded and there were less than 3000 psychiatrists in the country.⁴ It may be hoped that the awareness of and interest in nervous or emotional disorders increased and, in many instances, awakened by the present war will be maintained, both by physicians who are not psychiatrists and by laymen.

The aversion of the veteran to seeking psychiatric treatment is not difficult to comprehend. Society has looked askance at psychiatry for generations. Gregg⁴ refers to "the inherent, the inveterate, the inevitable handicaps of psychiatry." He writes, "The three most powerful traditions or historical heritages of psychiatry are still, as they have been from time immemorial, the horror which mental disease inspires, the power and subtlety with which psychiatric symptoms influence human relations, and the tendency of man to think of spirit as not only separable but already separate from body." Another handicap might be included. Neurotic and, to some extent, psychotic illness entails the question of personal responsibility, free will. Again and again the patient ill with neurotic symptoms expresses the wish that some physical cause might be found to explain his disability. At least half-consciously he fears to hear what he partly senses may be true, "It's up to you." Human pride or egotistic desire is such that it is difficult to admit that what is up to one may be more easily accomplished if one permits the doctor to help.

Government facilities for treating the veteran have not been, are not now and will not be adequate. It is well known that the veterans' hospitals have not been able to give satisfactory care and treatment to the casualties of World War I. Suggestions are

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being made that the federal government could contract for the care of veterans with the general hospitals Cunningham⁵ writes "Veterans are best treated in community facilities," thus precluding bureaucratic organization Terhune⁶ states

This problem is too big for the government to handle

If the government tries to care for these patients, after discharge from the Army, results will be unsatisfactory. The practice of medicine is based on an individual relationship existing between doctor and patient — this necessary personal emotional transference cannot exist between a government bureau and patient. Therefore, it will be the job of civilian physicians, who know these men and are familiar with the facilities of the communities in which they live, to readjust them to civilian life

Various writers have commented on the fact that the development of a nervous disorder under the circumstances of military service does not warrant the assumption that the man affected will be unsuited for at least a reasonably adequate adjustment to civilian pursuits Burlingame,⁷ in writing on industrial psychiatry, says

If a person is discharged from the armed forces with the diagnosis of psychoneurotic, it simply means that the individual did not have the necessary adaptability to become a successful employee of the armed forces. This diagnosis carries with it no adverse implication concerning that person's re-employability in industry

It is to be remembered that over a million men have been rejected in this country as not fit for service in the armed forces because of some neuropsychiatric disability. Again, exact statistics are not available, but it is known that the majority of these men were carrying on successfully enough in civilian life

If there is a correct understanding on the part of doctors and the public in general, most of the veterans who are nervous will readjust to life out of the service without great difficulty. Referring to the physician's treatment of the man who has not qualified for service, Terhune⁶ writes

Explain that they were not rejected, they were just not accepted for military duty, that this was for their own protection, and because they could be more useful to the Nation in other lines of endeavor. Reassure them about their own essential fitness for civilian life, pointing out that many of the qualities which make for a successful civilian do not necessarily make for a good soldier

If there exists, as part of man's response to his environment, a normal emotional reaction, — and outside of the psychiatrist's world, at least, it does exist, — then many of the fear and anxiety reactions engendered and precipitated by the indescribable conditions in combat zones cannot justifiably be labeled "psychoneurotic"

Thomas⁸ refers to the injustice of calling all manifestations of fear, anxiety and depression psychoneurotic. In reporting on 4 cases in which there was temporary maladjustment, he writes

They constitute a behavior pattern that has been witnessed in armies throughout the ages. Until the advent of modern psychiatry, such conduct was attributed to a variation in men's capacity to sever themselves from their

usual way of life and to conquer a fear of impending death. The will to fight, morale, training, fatigue, disheartening reverses and leadership were recognized as factors able to influence a man's emotions. These factors are acknowledged in this war, but the frequency with which the diagnosis of a psychoneurosis is made raises a suspicion that psychiatrists have encouraged a shrouding of them in an ill use of terminology. In doing so they have thrown the problem of psychoneurosis out of focus with what seem to be the facts. There are psychiatrists who regard the familiar fear of a soldier in a dangerous situation as a measure of the emotion of an anxiety neurosis. This is tantamount to calling all frightened and bewildered soldiers psychoneurotic. Careless use of the term ["anxiety"] does injustice to the Army, the soldier and the taxpayer

Thomas suggests the use of the term "simple adult maladjustment" when the ramifications of what a diagnosis of psychoneurosis implies are not present. He continues

It is obvious from what has been said that I believe that some of these cases present problems in morale, discipline and stamina. If this is so, it follows that any term connoting a mental disorder will cloud the issue. The answer to the question seems to rest in the prophylactic orientation program now under way — the prevention of states that require a stigmatizing name

This question of nosology is important because people generally are still not well educated in regard to nervous disorders. They forget the wisdom of the Quaker's statement that "Everybody is queer except thee and me, and sometimes I think thee is a little queer." At best the label of psychoneurosis is dangerous because it tends, in the mind of the person so labeled and in the minds of others, to distinguish and to separate him from the rest of the supposedly normal world

The psychiatric casualties of this war may be roughly divided into two groups, those suffered by men whose previous integration has been averagely sound and who have broken down due to intolerable circumstances, and by those whose histories reveal evidence of instability before the beginning of their military service. Prognosis is better for the first group, but it is probable that the second group comprises the larger number of the disabled. Rennie and Woodward⁹ report that of 380 cases seen at the Rehabilitation Clinic of the New York Hospital, 75 to 80 per cent gave a history of difficulty antedating service

The work of rehabilitation is not being left entirely to civilian and Veterans Administration resources. Both the Army and the Navy have already instituted treatment in the directions of both reconditioning and rehabilitation. Braceland,¹⁰ in writing of the Navy's project, says

It is encouraging to know that in this particular field the Navy has had a rehabilitation plan in operation for well over a year. This program has now expanded to such a degree that the basic idea of treatment and reconditioning is operative from the time the individual becomes a neuropsychiatric casualty on some Pacific atoll or island until the time he is considered recovered or is discharged to the Veterans' Administration facilities for further treatment.

Group therapy, according to the same author, is the method of choice

That group therapy is effective is the opinion of Dynes, Hamilton and Cohen.¹¹ They write that, although not all patients are cured, many have left the hospital with an unhostile attitude. They add

Many expressed a feeling that they had been treated fairly and had hopes and plans for the future. This contrasts sharply with those patients discharged from the service who return to their homes in an unhappy frame of mind and immediately become candidates for veterans' aid, instead of making an attempt to help themselves.

In the group discussions, as conducted by Dynes and his associates, the members were encouraged to describe their symptoms. The meaning and nature of symptoms were then discussed in relation to personality and its development, anatomy, physiology, emotions and their influence on mind and body. The authors say that the individual patient was not embarrassed, any particularly sensitive points being discussed privately.

In a description of the process of group therapy in an Army hospital, Paster¹² relates that it is usual for the aggressive, extroverted patient to express himself first.

The timid and the withdrawn then follow with comparative ease. It is remarkable how patients who, when individually interviewed, are reluctant to discuss their terrifying past change their attitude during the group sessions. Surrounded by other patients who manifest symptoms similar to their own, most of them lose their sense of inferiority. They talk much more freely about their painful experiences and reveal the inner turmoil they previously tried to repress.

The value of this therapy is evident in that 85 per cent of the men so treated have been returned to duty, although not as combatants. Part of the value, according to Paster, lies in the patient's finding that he automatically minimizes his personal problems as the latter become a part of the larger group problem. Also the presence of other patients helps to socialize each of them. Paster concludes

The favorable response of the patients to the comparatively brief period of treatment [two or three times a week for four to six weeks] corroborates the opinion of many that psychoneurotic reactions arising in combat are not generally deeply rooted. They do not fundamentally represent lifelong problems, but rather symptoms of acute maladjustment to intolerable situations.

Helpful as group or individual therapy may be to a man while he is still in service, partial or apparently complete restoration to mental or emotional health before discharge does not preclude difficulties in making the transition back to civilian life. The success or efficacy with which this adjustment will be made depends on the individual veteran's plasticity and emotional integration and various factors in the society to which he returns. One of the most important elements in this situation is the matter of compensation or pensions for veterans. Unfortunately, many men will accept government aid as long as it may be forthcoming, and thus neurotic reactions will become fixed either for life or for years.

Sinclair,¹³ of the Australian Army Medical Corps, who has had comprehensive psychiatric experience in the present war, admonishes

The nation is still paying for the neuroses directly or indirectly attributable to the last war. The burden following the present conflict will be far greater. The policy adopted after the last war was to pension the soldier and to treat him at a repatriation centre. It will be a great pity if we repeat that folly. There seems no doubt that to shackle the neurotic to his symptoms and disabilities by a monetary dole is a poor solution to his problem. Society will best support the neurotic repatriated soldier by giving him constructive, creative and sympathetic service, rather than by paying him a fortnightly pension in an endeavor to forget him.

What Terhune⁶ has to say on this subject is worth quoting.

The greatest hazard that exists in treating ex servicemen who are psychoneurotic is that they are eligible for federal pensions. Once these men have applied for a pension or have secured one, it becomes practically impossible to cure them. Few compensation neuroses recover as long as the compensation continues in effect. It is unfortunate that recent federal legislation makes these patients eligible for pensions, since this very fact will make many confirmed neurotics of individuals who would otherwise recover. Such federal provision was made without consultation with medical authorities familiar with the problem.

The author urges medical societies to fight for new legislation. In dealing with the veterans themselves, he advises the doctor to try to persuade them "not to apply for pensions, pointing out the nature of the risk and showing them that by accepting pensions they are selling their birthright of happiness and usefulness, dooming themselves to lifelong discomfort, all for a mere pittance."

The numerous psychologic hurdles standing in the way of the returned soldier's successful reorientation to civilian life have been well presented at length by Pratt.² He discusses the possible obstacles that may be present both in the veteran's attitudes and in those of his family and social milieu. Patience, forbearance and an unremitting attempt to understand are the keynotes for success.

Chisholm,¹⁴ in an excellent paper, outlining the Canadian Army's proposals for preparing its soldiers for demobilization, writes of some of the most important points related to rehabilitation. He says

Aggressive urges which have been carefully nurtured and developed over a period of years are supposed to disappear overnight, leaving a peaceful civilian with no such pressures and consequently no need of outlet. The soldier is expected overnight to give up what in very many cases at least is a consuming hatred and in all cases the object of aggressive antagonism. With the memory of his friends or relatives who have been killed or maimed or even tortured by the enemy, fresh in his experience and kept alive as a spur to his aggressions, this change-over in attitude may be very difficult indeed. It may be successful on the surface but at the expense of extensive repressions and conflict within himself.

The well-known tendency of the soldier at war and the wife at home to idealize each other, with perhaps consequent disillusionment, fears of what may or may not have been infidelity, idealization of the father by the mother to the children, at

variance with the real father on his return, the wife's independence, personally and financially, in relation to her husband, while he has been away, the wife's experience in war work, having broadened her horizon beyond the domestic round, the matter of re-employment or employment for the first time in a civilian job for the returned soldier — all or some of these situations may be the source of difficulties. According to Chisholm, the Canadian Army's plan is an attempt to make the soldier's transition to civilian life less uncomfortable and, as so often happens, disillusioning by courses of lectures and discussions in small groups on all conceivably pertinent subjects.

The working and suffering together and the value of their efforts to their countries have given to many soldiers a well deserved self-esteem that may never have been experienced by them before to such degree. The doffing of the uniform and the return to a position of relative unimportance can be a serious threat to healthy adaptation unless families and the community remember that the wisest form of appreciation goes farther than an initial flag-waving reception. In another paper, Chisholm¹⁵ comments on this

For some years the soldier will have been accustomed to regarding himself as important, as a great asset to his country and as highly valued by his associates. The most damaging thing that could happen to the returned soldier and to the community to which he returns would be for him to find himself not wanted and not regarded as a valuable asset to the community. To give him money or even to provide him with a stopgap job will fall far short of these requirements. In order for him to become a useful civilian citizen it is very necessary that his own individual value to the community should obviously to him remain high. This will require very careful planning and very generous and serious implementation.

Community responsibility is stressed in the literature on rehabilitation. There is much exhortation about it. Rennie¹ writes, "The whole purpose of psychiatric treatment may even be defeated by the unresponsive or negativistic attitude of the community or industrial employers." Rennie and Woodward⁹ are convinced that

The degree of social adjustment that men returning from the armed forces make and the speed with which they do it depend to a very real degree on the understanding they find among civilians, and on the way the people at home treat them. With understanding, reassurance, and constructive treatment, many of them achieve an acceptable status and carry on quite effectively after an adjustment period of a few weeks or at most a few months.

Farrell¹⁶ also believes that the tasks of rehabilitation are not singly those of the medical profession. He adds

Business also has a large measure of responsibility. They must be given every chance and encouraged to make good in industry. It is often remarkable how quickly even some of the most upset individuals return to their former life and efficiency in their productive work once the pressure that broke them can be removed.

The psychiatrist should take the lead, in the opinion of Finesinger and Lindemann,¹⁷ in organiz-

ing community resources. They write, "An educational program making available what we have to say to the general medical profession, to community authorities, social agencies, industrial personnel and clergymen should be the concern of our intensive thinking." They state that rehabilitation clinics are rapidly developing in different communities.

As suggested earlier in this review, one of the problems of rehabilitation is the disinclination of men needing help to seek it. Community efforts will have to be enticing to attract the veterans who are not desperate, or not unusually well educated in regard to mental hygiene, or not dependent enough to want and to accept what is offered. Millet¹⁸ is sanguine in this regard. He writes

Fortunately, large numbers will have highly constructive or hopeful attitudes toward their disabilities and be eager to take whatever specific retraining is necessary in order to be able to resume a life of self-support and independence. Such men may be counted upon to broaden the understanding of civilians as to the needs of other discharged men, and in some cases will provide excellent material for recruiting as experts in rehabilitation.

In spite of Braceland's¹⁰ charge, "It has been repeatedly stressed by industry as well as by the military services that a man must be fit for all duties or for none at all, and this all or none theory is the psychologic barrier which the returning veteran has to hurdle," it is to the credit of psychiatry and industry that for some years the larger industries, at least, have recognized the value of including psychiatrists or psychiatrically trained personnel directors on their staffs. Employment and employee-employer problems and the personality of the individual worker, as contrasted with the impersonal, exclusively monetary profit motive, had been given consideration and attention from the psychiatric or mental hygiene point of view long before the industrial rehabilitation difficulties of World War II arose.

The principal hazard in the present situation is that industrialists may be influenced by the popular articles of journalism to believe that it is well to be wary of the man who has been discharged for neuropsychiatric disability. How a division of the General Motors Corporation is meeting the issue of rehabilitation in industry is well delineated by Smith.¹⁹ He wrote in April, 1944, that the Delco-Remy Division had been keeping in touch constantly with about 5000 employees in military service. These men were sent letters, and gifts on various occasions, as at Christmas and Easter, and were told that they were wanted back when the war was over. Hundreds of letters had been received each week from the former employees. "Every letter that asks a question or indicates that a reply is desired is answered."

The policy of the Delco-Remy Division is as follows

Veterans will be given every possible assistance, sympathy, and consideration in helping them to get back into

the normal swing of civilian life. However, it is not our intention to oversympathize, coddle or lead them by the hand. In our opinion such treatment will simply lead to untold trouble in the future, as it develops in the individual the feeling that he is different from other people, entitled to special considerations, and that the world owes him a living.

This policy includes the decision not to give veterans preferential treatment. Although the plan of setting them apart from the general group of employees was considered, it was decided "that the veteran should, to all outward appearances, be treated as all other incoming employees." Smith states that a great majority of over one hundred veterans questioned on this plan preferred to be considered as no different from their fellows. This is the particular desire of that group of veterans who have been discharged from military service because of some slight mental or physical impairment which made them unfit for life in the service.

At the time Smith's report was written the Delco-Remy Division had employed 475 veterans. It was found that these men fell into two general classes. The first comprised battle-incurred disability discharges and men discharged as unfit for service because of some slight mental or physical disability. The rehabilitation of this class had not proved much of a problem and it was thought it would not in the future. The second class was made up of men who had been discharged because they were temperamentally unsuited for military service. Smith states, "This is the group who are emotionally unstable, and in the vast majority of these cases these characteristics were not acquired in the service but are inherent."

Smith's analysis of this type of veteran and the troubles he initiates is perspicacious. This man was a problem before the war, and now that he is a veteran he is more of a problem than ever, taking advantage of being classified as a veteran. He decidedly wants preferential regard. He can do no heavy lifting because of back injury.

He has calcified glands in his chest and objects to working in any dusty environment, he has an alleged heart condition and must do extremely light work, or he has defective feet and must sit down. He is the "misfit," and generally you will find that he was a "misfit" in society before he entered the service.

The author sees him as a potential danger to the industrial rehabilitation program. Since the man draws and necessitates attention and supervision, there is the danger that he may become a false symbol of the whole body of veterans. Smith believes that industry does owe these men a fair chance. "We will go even further with them than we would with the ordinary employee." He rightly enough thinks, however, that their rehabilitation is not basically industry's but that of society as a whole. He cautions that it is in relation to this type of veteran that pressure groups may arise. A union may charge that big business is being unfair

to an ex-soldier when actually industry is doing all that it can to help an incompetent. Smith concludes

The number of veterans who return with physical or mental impairment will be relatively small in relation to the total in service. This job resolves itself to simply handling each case on an individual basis, taking into consideration capabilities as well as limitations, assisting him to choose the work which he will be able to do best in order that he may be a self-sustaining member of society for the balance of his productive life, doing all this without emotionalism or paternalism — helping him to help himself.

If industry throughout the country could carry out the purported policy of the Delco-Remy Division, it would seem that the veterans' reinstatement would be wisely directed.

To help industry, especially the small and moderate-sized companies, which employ the major portion of American labor, in the work of readjusting service men and women to industrial jobs, the Subcommittee on Psychiatry of the National Association of Manufacturers Medical Advisory Committee has prepared a pamphlet, *Readjustment to Civilian Jobs*. The pamphlet is for distribution to management and contains an explanation of what neuropsychiatric disability means, suggestions for placement interviews and a plan for classification and placement in accordance with the psychiatric and personality impression given by each applicant.

The pamphlet is designed for use not only with the ex-service man but also with the demobilized war worker. It reads in part

It is possible that the greater problems will come from the ranks of these war workers. These war industry "employment neurotics" were the product, primarily, of emotional difficulties arising from their failure to adjust to employment requirements and, in many instances, although to a lesser degree, to their failure to adjust to abnormal living conditions in war industrial centers, and to new and unusual social relationships. In attempting to solve their emotional problems, the war-industry neurotics shifted their jobs in large numbers.

The plans for placement consist of estimating the applicant's personality, abilities and disabilities, carried out by a consulting psychiatrist or personnel director, or, if neither of these is available, by the company doctor or the applicant's own doctor, in conjunction with members of the managerial staff, also temporary job placement, providing for "a period of mutual 'on-the-job observation' between the applicant and the employer," when there is doubt about the worker's stability or capabilities.

Comparatively simple as all this may seem, if industry generally could be made aware of the possible value of psychiatric screening and direction, postwar employment difficulties would at least be ameliorated.

There is much literature for public guidance on how the returning service man and woman should be treated. One of the shorter of these, *When He Comes Back and If He Comes Back Nervous*,²⁰ is suitable for families who may want suggestions or

advice Besides explaining briefly how and why war experience may change the man who has been in service, it contains a number of sound "do's" and "don't's" Also, Pratt's² book, referred to previously, contains a large amount of generally useful information

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

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CASE 31291

PRESENTATION OF CASE

A sixty-one-year-old man was admitted to the hospital because of fever, chills, malaise and weight loss

The patient had been well and active until about four months before admission, at which time he began to feel weak and tired He had sudden chills and fever and remained in bed for several weeks He took small doses of quinine without consulting a physician Three months before admission he developed severe spontaneous nosebleeds, for which he was admitted to a community hospital, where he remained for three months While at the other hospital he ran a septic course, with a chill and a sharp temperature rise to about 103°F almost every afternoon It was necessary to pack the nose because of repeated spontaneous hemorrhage The red-cell count fell from 3,300,000 on admission to 2,400,000 at the time of discharge The white-cell count varied from 7000 to 15,000, with as many as 93 per cent neutrophils A platelet count was 65,000, the bleeding time 2¼ minutes, the clotting time 3¾ minutes, and the prothrombin time 20½ seconds A tourniquet test was negative The

*On leave of absence.

urine was normal The serum nonprotein nitrogen was 30 mg per 100 cc The Hinton and Wassermann tests were negative X-ray and physical examinations of the heart and lungs were negative One blood culture showed diphtheroids Several blood cultures showed *Staphylococcus albus*, and two cultures yielded colon bacilli Examinations for malarial parasites were repeatedly negative Tests for agglutinins against typhoid, paratyphoid and dysentery bacilli were negative He was given sulfadiazine until it was learned that the *Staph albus* grown from the blood was resistant to sulfonamides He was given up to 20,000 units of penicillin every hour for several weeks During penicillin therapy the blood cultures became negative, but he continued to have chills and a fever of 103°F The teeth, sinuses, nose and throat and the genitourinary system were thoroughly studied by consultants and were said to be negative An intravenous pyelogram was normal X-ray films of the bones were normal Penicillin was stopped, and the blood culture promptly became positive for *Staph albus* Sulfadiazine was given in high dosage, and a blood level of 15.2 mg per 100 cc was obtained After two weeks the sulfadiazine was stopped because of hematuria, crystallinuria and a nonprotein nitrogen of 72 mg per 100 cc Fluids were forced and the patient became edematous, whereupon the fluids were limited The urine soon became negative Considerable abdominal discomfort, of which he had begun to complain, was relieved by enemas The blood cultures remained negative after the administration of the second course of sulfadiazine until three days before he was discharged, at which time *Staph albus* was again obtained Shortly before discharge the serum albumin was 2.15 gm, and the globulin 3.75 gm per 100 cc, an albumin-globulin ratio of 0.57 This test was repeated, and the albumin was 1.84 gm, and the globulin 4.16 gm At the same time the serum nonprotein nitrogen

was normal, and the sedimentation rate 14 mm per minute. X-ray films showed marked gaseous distention of the intestines, with a high diaphragm, especially on the right. The temperature varied from 100 to 106°F. Many moist rales were heard in the chest posteriorly. He was transferred to this hospital in an ambulance.

Physical examination revealed a thin, pale, drowsy man who appeared chronically ill. There was moderate pitting edema over the sacrum and of the lower extremities. Respiratory excursions were shallow. The diaphragm was high on both sides. There was dullness at both bases posteriorly, considerably more marked on the left than on the right. Breath sounds and vocal and tactile fremitus were markedly diminished at the left base. Moist crepitant rales were present at both bases. The heart was slightly enlarged to the left. The rate and rhythm were normal. No murmurs were heard, and the aortic second sound was equal to the pulmonary. The abdomen was markedly distended but not tender, there was shifting dullness, but no fluid wave could be elicited. The liver and spleen could not be felt.

The temperature was 99.0°F, the pulse 90, and the respirations 23. The blood pressure was 165 systolic, 105 diastolic.

Examination of the blood showed a red-cell count of 2,400,000, with 7 gm. of hemoglobin, and a white-cell count of 9800. The differential showed 78 per cent neutrophils, 17 per cent lymphocytes, 3 per cent monocytes and 2 per cent eosinophils. The stool was brown, formed and guaiac negative. Serum and spinal-fluid Hinton tests were negative. The urine was cloudy, had a specific gravity of 1.014 and gave a + test for albumin, the sediment contained 3 or 4 red cells, 12 to 20 white cells, with occasional clumps, a rare granular cast and many bacteria per high-power field. An abdominal paracentesis yielded 2800 cc. of light-yellow, slightly hazy fluid. The specific gravity was 1.008, and the sediment contained 115 white cells (mononuclears) and 45 red cells per cubic millimeter. A culture showed no growth. The serum nonprotein nitrogen, chloride and carbon dioxide levels were normal. The protein was 5.13 gm. per 100 cc., with an albumin-globulin ratio of 0.9. The cephalin flocculation test was ++++ in twenty-four hours. The prothrombin time was 24 seconds (normal, 18 to 20 seconds). A bromsulfalein test showed 60 per cent retention forty-five minutes after 5 mg. of dye per kilogram of body weight had been injected. A blood culture yielded no growth. The urine grew abundant colonies of colon bacilli. An x-ray film of the chest showed the right half of the diaphragm to be high in position, but both sides moved well. The liver was thought to be considerably enlarged. There were areas of increased density in the right middle and lower lobes. The heart was prominent in the region of the left ventricle. A gastro-intestinal series was negative.

The patient felt weak and frequently became flushed. The paracentesis relieved him completely of a moderate amount of dyspnea. He ate poorly, frequently refusing a meal. He was given four transfusions and frequent intravenous injections (dextrose, Amigen and physiologic saline solution). During the first week he showed a low-grade fever, the temperature rising to 101°F every evening. During the second and third weeks the fever was more erratic, with daily spikes sometimes reaching above 103°F. The pulse and respirations spiked with the temperature.

On the third day the liver was palpable two finger-breadths below the costal margin. On the fourth day the patient complained of a stiff neck. A lumbar puncture revealed normal spinal fluid, except for a gold-sol curve of 5554333100. Peritoneoscopy showed a normal-appearing liver that did not seem to be enlarged, the peritoneum was smooth. A liver biopsy showed no abnormality.

On the tenth day he again became markedly dyspneic. On the following morning he complained of sharp pain in the right chest anteriorly. The right dome of the diaphragm was found high and considerably more elevated than the left. Breath sounds in the right lung field were markedly diminished, and a moderate number of fine moist rales were heard. Examination of the legs was negative except for edema. An abdominal paracentesis yielded only 100 cc. of fluid. An x-ray examination of the chest showed considerable change since the observations made shortly after admission. The right lower lung field was diffusely hazy, and there was evidence of fluid within the pleural cavity. It was impossible to determine the position of the right leaf of the diaphragm. At the same time the urine contained innumerable white cells, many in clumps, and bacteria. The white-cell count was 36,500, with 9 gm. of hemoglobin. The stool was for the first time guaiac positive. There was no pain or tenderness in the abdomen or back.

On the sixteenth day the patient became incontinent and spoke in a disoriented fashion. Weakness and weight loss progressed. After several transfusions the serum protein was 6.1 gm. per 100 cc. The nonprotein nitrogen, chloride and van den Bergh remained normal. The white-cell count on the twentieth day was 21,000, with 94 per cent neutrophils. He became severely dyspneic again and slightly cyanotic and was relieved somewhat by an abdominal tap, which yielded 1800 cc. of thin yellow fluid. No fluid was obtained by thoracentesis.

On the twenty-second day the chest began to fill with fine rales and wheezes. Severe dyspnea returned. The pulse was 120. He was digitalized rapidly with Cedilanid. When pulmonary edema became alarming, he was given oxygen and tourniquets were applied to the extremities. The following morning he went into peripheral collapse and expired.

DIFFERENTIAL DIAGNOSIS

DR WYMAN RICHARDSON As usual I have two possibilities in mind Was this primarily infection or primarily tumor, possibly with secondary infection? This time I am going to rule out tumor as a primary cause of the disease because the only one I can think of as a possibility is lymphoma, and the whole course of the disease seems to be more that of infection The thing that bothers me a little is the rapidly increasing anemia in the beginning, which is perhaps more than one would expect with ordinary infection, although it is possible

This case brings up the question of how much to believe the evidence from a hospital with which we are not familiar. I do not wish to be "stuffy" about that, but when one is around a hospital, one realizes the difficulties of the laboratory and has opinions about the methods employed and whether or not the laboratory procedures can be considered important or reliable There is some discrepancy between the laboratory findings at the other hospital, and one finding in particular, the positive blood culture for *Staph albus*, deserves attention *Staph albus* showed up with great regularity when the patient was in that hospital In this hospital, apparently the physicians in charge were not too interested in the blood cultures because only one is noted, at least in this protocol, and that was negative So I am left a little in doubt whether to take the finding of *Staph albus* seriously It is a frequent contaminant On the other hand if it appears in two flasks regularly, following a rigid technique, one has to believe it. The question is, When does one begin to believe it?

The other thing that I want to comment on in regard to the original laboratory work is the platelet count of 65,000, with a normal bleeding time and tourniquet test I teach the students in the course in laboratory diagnosis that the platelet count is not worth doing I believe that is true The reports of technicians who have spent a lifetime doing these counts are of some value, but as they are usually done they cannot be depended on One can look at blood smears, if the platelets are diminished, allowance being made for the number of red cells, one can arrive at some definite conclusion When the platelets are normal in number they clump and cannot be counted I do not believe that the platelet count of 65,000 is important

This whole story sounds primarily like infection to me We might try to tackle this problem from the organs chiefly involved, that is, the kidneys, liver and lungs The x-ray studies of the lungs at the first hospital were negative, but later there was something that suggested difficulty involving the chest. Involvement of the kidneys appeared right after the patient had been on sulfadiazine for a considerable period of time, and involvement of the liver came on after that period, so that one begins to think of the possibility of some sort of infection, perhaps complicated by the use of large

amounts of sulfonamides That is about as far as I can go with the case I have come to a conclusion in regard to what this infection might have been, but I think that I should like to look at the chest plate now I might say that what I am thinking of is whether this man had thrombophlebitis with septic infarcts, whether he had phlebothrombosis with noninfected infarcts, whether he had multiple abscesses in the lungs, whether he had pulmonary tuberculosis or some such process or whether he had atelectasis from a high diaphragm

DR GEORGE W HOLMES I think that we can rule out a few of the possibilities I do not believe there is any evidence of miliary tuberculosis or anything resembling it I do not believe that he had miliary abscesses in the lungs, or abscess of any kind There is a high diaphragm on the right side, if one can believe the report that it moved freely, it was probably due either to a large liver or to some degree of atelectasis There is a line running out just above the diaphragm that could be the end result of localized atelectasis, but it is not definite The heart, I think, is perhaps within normal limits Because of the high diaphragm on both sides the heart lies horizontal in the chest and therefore seems larger than it is The curve of the left ventricle is a little prominent, and he may have had some enlargement of the left side of the heart The aorta shows tortuosity, but no more than what a man of his age should have. There is no calcification in the walls, and no evidence of mediastinal tumor

The films taken about a week later show increased density on the right side of the chest and what looks like fluid in the pleural space, perhaps with consolidation in the lung fields One wonders if this could have been a terminal affair The left lung still shows no essential change The heart has rotated a little so that it may be slightly displaced, but I doubt it Evidently this film is an attempt to see whether or not he had esophageal varices There is no evidence that he had them There is nothing in the examination of the stomach, it was said to be negative, and what films we have confirm that

DR RICHARDSON I am still in a quandary Incidentally, we have no history of injury to account for a portal of entry for this organism, which is important Dr Castleman tells me that the patient was a Greek, born in Greece What was his occupation?

DR BENJAMIN CASTLEMAN He was in the tonic business

DR RICHARDSON Perhaps he took too much of his own tonic Some Mediterranean people have a tendency to liver disease I do not believe that we have to consider echinococcal disease in this case

So it comes down, as far as I am concerned, to a blood-stream infection without any obvious portal of entry to account for the illness before he arrived in this hospital, and I am inclined to take the blood culture of *Staph albus* seriously in that it appeared

to be somewhat affected by therapy I think that the history suggests that he had pulmonary infarcts. We know that a partial collapse of the right lung base, with fluid, is not an infrequent finding in the presence of abdominal fluid and liver disease, and that may be the whole explanation. We know that he had a urinary-tract infection and have to say that he had a pyelonephritis. The question is whether that is the only lesion or whether there are others.

I am still trying to decide whether he had thrombophlebitis from the onset. I think that I shall accept *Staph albus* septicemia as the diagnosis in the first hospital, as a result of the septicemia, he may have had abscesses elsewhere, including renal abscesses. I believe that he was given sulfonamides in proper doses, but he had had them for such a length of time that toxic effects may have occurred, therefore I shall have to bring up the question of a toxic effect on the kidneys.

Finally, one has to explain the liver. There is no evidence of liver infection that I can see. There seems to be evidence of diffuse involvement of the liver. I might parenthetically state the evidence for that: a 60 per cent retention with a large dose of bromsulfalein, a ++++ cephalin flocculation test, a reversal of the albumin-globulin ratio, with a quite marked increase in the globulin at the other hospital (the total protein had gone down when he reached this hospital, but he still had increased globulin here), slight increase in the prothrombin time (probably of no significance), and ascitic fluid that was a transudate rather than an exudate. It is possible to suggest that this man had a toxic involvement of liver as a result of the sulfonamides. It is, however, a rather rare condition, and I assume that this man had some underlying liver disease to start with.

I shall say specifically that this man had a bloodstream infection, possibly due to *Staph albus*, pyelonephritis, possibly multiple abscesses, pulmonary infarction and toxic hepatitis superimposed on cirrhosis.

DR J H MEANS We struggled with this diagnosis in much the same way that Dr Richardson has. The patient was desperately ill when he entered, although he was not running a fever. Later he ran a septic fever. In my first note, I said "I cannot make a diagnosis. He has, I believe, some undrained pus somewhere. At least it must be searched for. There is considerable evidence of liver involvement. He could have a liver abscess." Then we thought of lymphoma, and I stated farther along that the studies were indicated, especially of the liver. Just as Dr Richardson thought, because of the 60 per cent dye retention, the ++++ cephalin flocculation test, the low albumin-globulin ratio and so forth, I made this note, "If it is cirrhosis, the hair-on-the-chest rule will have been broken because he has plenty of it." A liver biopsy was said to be negative. Still later I wrote that the

patient had been running a fever since the punch biopsy, had a leukocytosis and had developed right pleural effusion, and I wondered if there was any relation between the procedure and the subsequent events. We never established that there was. I begged the surgeons to search for pus somewhere, but I could not sell the idea to them. That is as far as we got.

The final diagnoses were liver disease and urinary tract infection, we thought that the signs in the lungs were due to pulmonary edema. We investigated the urinary tract, colon and gall bladder in the hope of making a diagnosis, but that is as far as we got. We thought that he had liver abscess in all probability. He did not have meningeal signs, and a lumbar puncture was negative. Dr Benedict saw no peritoneal lesions when he did the peritoneoscopy, and he could not establish anything in the lymphoma category.

This will turn out to be an interesting case. I know that it brings up the point that one will not make the correct diagnosis unless one thinks of all the possibilities. The past history was talked about a little, but insufficiently. We obtained no history of what would have given the clue to what the pathologist found. If we had gone at it harder and perhaps more expertly, we might have got it, but the patient was said to have been well until the sequence of events that led to his death began.

DR FRANCIS D MOORE At the time that I saw this patient the problem was whether he had right subdiaphragmatic abscess, either secondary to some focus that was back of the whole disease picture or secondary to peritoneoscopy, following which he developed more fever. It was difficult to settle the matter one way or the other. He did not have much tenderness in a region of the right eleventh and twelfth ribs and there was none in the upper quadrant. As a matter of fact, in relation to the final proved diagnosis, the absence of abdominal signs in either hospital, other than the signs of fluid, was interesting. At the time that I saw him I was not sure that he did not have subdiaphragmatic abscess. He was much too sick to explore.

DR MEANS I was not being critical. We thought it was good judgment on your part. I am trying to throw out the thought that we did bring up the possibility that he had pus that could have been drained and asked the surgeons about it. We could have been criticized had we not done so. At entry he had some suggestion of ileus, but it did not amount to much.

DR RICHARD H SWEET Was there any history suggesting antecedent appendicitis?

DR MEANS None that we could obtain.

CLINICAL DIAGNOSES

Pyelonephritis
Liver disease (? abscess)
Pulmonary edema

DR RICHARDSON'S DIAGNOSES

Septicemia (? *Staph albus*)
 Pylonephritis
 Multiple abscesses?
 Pulmonary infarction?
 Toxic hepatitis, with underlying cirrhosis?

ANATOMICAL DIAGNOSES

Periappendiceal abscess, chronic
 Peritonitis, acute fibrinous, pelvic
 Thrombophlebitis of superior mesenteric, splenic
 and portal veins (pylephlebitis)
 Liver abscesses, multiple
 Pancreatic abscesses, multiple
 Abscess, lesser omental sac
 Ascites
 Bronchopneumonia

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN The autopsy on this man showed a lot of fibrin and pus in the pelvis that was well on its way to organization. The upper abdominal cavity contained about a liter of clear fluid. The liver was slightly enlarged, and between the head of the pancreas and the right lobe of the liver was a large abscess that extended into the pancreas. Smaller abscesses were scattered throughout the entire pancreas. When the liver was sectioned we found two or three large abscesses, but the most striking finding was in the venous system. The main portal vein and all its radicles were filled with pus and purulent thrombi. These thrombi had extended into the splenic and superior mesenteric veins. We looked then, of course, for the appendix, since it is well known that pylephlebitis is most frequently caused by acute appendicitis. The appendix was extremely small and covered with fibrous tissue and rather porky, fatty tissue. There was no evidence of acute inflammation, but we thought that it might well have been the source of the pylephlebitis a month previously. Microscopically the appendix showed a chronic process. It is conceivable that the abscesses in the pancreas might have had something to do with the production of the pylephlebitis, but I rather think they were secondary to the abscesses in the liver. There was a pyelitis and a mild pyelonephritis. The lesions in the lungs proved to be bronchopneumonia.

DR. RICHARDSON What was the organism?

DR. CASTLEMAN We cultured the abscesses of the liver and found nonhemolytic streptococci and *Staph albus*, and from the blood we obtained nonhemolytic streptococci and colon bacilli. I think that perhaps the staphylococcus was not a red herring.

DR. MOORE This boils down to the question whether acute appendicitis can give pylephlebitis without rupture or without being gangrenous.

DR. CASTLEMAN The appendix might have ruptured. It was extremely small, and we could not find a definite tip. It is possible that the tip had completely organized over a period of several months. The fact that the infection that we did find in the abdominal cavity was located in the pelvis points more to the appendix than to any other organ. There were several loops of small bowel adherent to the exudate in the pelvis, but there was no abnormality in the intestinal tract.

DR. MEANS I should like to ask the surgeons whether anything could have been done if the diagnosis of suppurative pylephlebitis had been made when he first came in.

DR. SWEET Nothing, unless one is dealing with a large single abscess, which is not the case in pylephlebitis.

CASE 31292

PRESENTATION OF CASE

A twenty-day-old male infant was admitted to the hospital because of vomiting and diarrhea.

The infant was born at term, weighing 7 pounds, 2 ounces. The delivery lasted one hour. The mother said that the baby had vomited before it was discharged from the maternity hospital but there were no other feeding difficulties. At home the formula consisted of 12 ounces of whole milk, 10 ounces of water and 3 tablespoons of Karo. Vitamins A, C and D were given in adequate amounts. The baby fed well but vomited each feeding a few minutes after it had been taken. The parents were not certain that the vomiting was projectile. Proper belching did not prevent vomiting. The infant had six to seven bowel movements a day, which were green and liquid. The mother stated that the baby had had a rash on the buttocks when he left the hospital and that she thought that he had had diarrhea while in the hospital. Two days after the baby arrived at home, his formula was changed to skimmed milk and water, with no improvement. A few days later Dextrin-Maltose was added, to be omitted again after a few days. The baby had lost 1 pound, 2 ounces, before admission.

Physical examination revealed a dehydrated infant who was ashen gray. The anterior fontanelle was sunken. The child measured 20½ inches and weighed 6 pounds. There was a marked rash on the buttocks. The ears, nose and throat were normal. The lungs were clear to percussion and auscultation. The abdomen was soft, and the umbilicus showed a slight serous discharge. Peristalsis was normal. No masses were felt. The extremities were normal.

The temperature was 99.0°F, the pulse 130 and strong, and the respirations 34.

Examination of the blood showed a red-cell count of 4,500,000 and a white-cell count of 18,700. The stools were liquid and green and contained no blood. The urine was normal. The blood was Type O,

Rh+ The serum nonprotein nitrogen was 22 mg per 100 cc, and the protein 3.4 gm

The child was given nothing by mouth, being fed parenterally. He was started on sulfadiazine as soon as hydration was established, and from the next day on he was also given penicillin. He continued to have small green stools. A lumbar puncture was negative, and culture of the cerebrospinal fluid showed no growth. After forty-eight hours on parenteral-fluid therapy, he was given skimmed milk and Karo by mouth. Within ten hours the number of stools increased to such an extent that these feedings were promptly discontinued. No pathogenic organisms were grown from the stool. A culture of the discharge from the umbilicus grew colon bacilli. A blood culture on admission was contaminated, and one on the fifth day showed no growth. Cultures from the nose and throat showed chiefly *Staphylococcus aureus*. The sulfadiazine level, based on two determinations, was about 5.0 mg per 100 cc.

The child seemed greatly improved on the fourth day. Physical examination showed that he was well hydrated. The nose, throat, ears, lungs and urinary tract were negative for signs of infection. The rash on the buttocks had cleared, and there were three small dark green stools that day. The temperature had continued to be normal since admission.

The next morning the child suddenly became cyanotic and went into circulatory collapse. The extremities were cold. The respirations were 22 but were labored, with some sternal retraction. The heart sounds were of poor quality. The abdomen was distended, and the liver was not enlarged. Peristalsis was normal. The stools, which had been guaiac negative, became positive. X-ray examination of the chest and abdomen was negative. The child was given plasma, 10 per cent dextrose in water and physiologic saline solution intravenously and was placed in an oxygen tent. The white-cell count on the fifth day was 3250, with 75 per cent neutrophils, the hemoglobin was normal. Three hours before death, bilateral swelling was noted over the mastoid region. The eardrums appeared normal. The temperature, pulse and respirations continued to be normal. The child expired quietly on the evening of the fifth day.

DIFFERENTIAL DIAGNOSIS

DR DARIO MORELLI Before we attempt to arrive at the cause of vomiting and diarrhea in this infant, I should like to comment on one point which to me is exceedingly important and which has been omitted, that is, the details of the birth. A great deal of information can be derived from points concerning the type of birth, the condition of the baby at birth and the immediate postnatal as well as the neonatal period. We are told that the infant was born at term and weighed 7 pounds, 2 ounces, and that the delivery lasted one hour. This is quite a

long time for delivery, unless it is meant to indicate the whole period of labor. Obviously they must have had some difficulty in the delivery of this child, if delivery is interpreted as the second stage. It was probably a dystocic one, and the possibility of some injury in the process of being delivered has to be kept in mind. We do not know, however, what the condition of the baby was immediately following birth, and so far as the neonatal period is concerned, we have only some vague statements from his mother. She thought that the child might have vomited and that he might have had diarrhea while in the hospital.

At home the vomiting increased to such an extent that he was vomiting after each feeding and the diarrhea was rather marked. The various causes of vomiting in an infant vary from trivial conditions to some which represent serious disease. I am sure that we can rule out most of them very easily.

Air swallowing is one of the very frequent causes of vomiting and that mechanism is quite clear. If the baby swallows air during the taking of food, the air bubble is quite readily expelled and may bring with it food previously ingested. Also, too frequent feedings or too large a volume of food given at one time may cause vomiting. Undue manipulation, improper handling of the baby and unsuitable composition of food have been mentioned as causes of vomiting. Then we have vomiting due to obstruction, such as pyloric stenosis, or obstruction in the intestine, such as intussusception or atresias in the duodenum or in other portions of the intestine. Allergy, pyloric spasm and intracranial lesions are also responsible for vomiting in children. In evaluating the causes of vomiting in this child, his feeding seems to have been adequate and the formula well constituted. We do not know the interval between feedings but we assume that they were offered every three or four hours. The child was apparently "bubbled up" carefully. We can rule out air swallowing even if he did swallow air, the mother took care in getting it out of the stomach. We can rule out pyloric stenosis; there was no visible gastric peristalsis, the vomiting was not known to be projectile, and there was no constipation. Intestinal obstruction seems unlikely in that he was having a great number of stools, furthermore, the course of the child's illness certainly does not suggest it.

So we are left with two possibilities, an intracranial condition and a parenteral infection. Parenteral infections are often the cause of vomiting in childhood, especially at the onset of the condition. Before we go any farther with the vomiting let us consider the causes of one of the other symptoms that this child presented, that is, the diarrhea. Unsuitable composition of the food is one. There are a great variety of specific enteric infections, such as bacillary dysentery, typhoid fever and paratyphoid fever, and there is also the extremely im-

portant group of parenteral infections that cause diarrhea in the newborn or in the small child. It immediately emerges from these few considerations of the possible cause of vomiting and diarrhea that we have one condition common to both — parenteral infection. As a matter of fact he was so treated after he first came to the hospital. Very wisely they hydrated him before starting sulfadiazine. The sulfadiazine was followed by penicillin. There is no question that the attending physicians were thinking in terms of infection, and they instituted a careful search for the location of the infection. Apparently the upper respiratory tract was normal. The urine was negative. The ears, throat and nose were said to be normal, although some reservation can be made at this point. I do not doubt the sincerity of the observation but it is known that examination of the throat and ears in a dehydrated infant is certainly a difficult task, not so far as accessibility is concerned but because the appearance of these structures may be quite changed by the dehydration and the throat may not appear infected when it is. We know that often even the most experienced observers have difficulty in deciding whether or not the throat is inflamed in any given case. The same can be said in reference to the ear. Apparently this baby was treated for infection, and the likeliest one was parenteral. The stools did not grow any pathogenic organisms.

Another interesting point is that he had a discharge from the umbilicus. A moderate discharge from the umbilicus is often seen and may be totally insignificant. Certainly a minimal amount of infection is present in a great number of infants and does not constitute any threat to the child's health. It is only when there is infection that spreads to the neighboring tissues causing cellulitis, when this has happened, if the umbilical veins are not fully thrombosed, as in the first two or three days of life, infection may spread through them and cause a general sepsis and involvement of the peritoneum. However, the growth of colon bacilli in a culture from that discharge is probably not significant, but it may indicate something more important than what we are willing to ascribe to it. It is unfortunate that the blood culture on admission was contaminated. It would have been of tremendous importance in deciding whether or not he had sepsis. It was repeated on the fifth day, but by that time the child had received quite a bit of penicillin and one wonders if a positive culture had been affected by the treatment.

The rash on the buttocks is to my mind not specific. It is not described and is only classified as marked. It may have been due to the enormous number of stools that the child was having. It may have been the expression of a simple "diaper dermatitis." The rest of the skin was apparently normal. The rash, however, cleared up after the baby had been in the hospital for four days. One

wonders if better care had contributed to that improvement. I think the crux of the whole case is deciding whether this baby had an infection and, if he had, whether it was a parenteral infection or an infection somewhere else, also, whether he had a birth injury, and finally, what caused the baby's death.

I have little doubt that this baby had infection, with vomiting and diarrhea, and it gives me courage to note that in the hospital they apparently thought the same way and treated him for infection. The possibility of birth injury is suggested to me by the fact that delivery lasted one hour. If it was a breech delivery one could speculate on the possibility of intracranial injury, as well as injury to the adrenal glands. At least it is an interesting point to consider. We finally come to the fact that the child had apparently been almost cured. On the fourth day the baby was greatly improved; he was well hydrated, and he did not show anything wrong on physical examination. The stools were few, although the abstract does not say whether they were loose or were formed, possibly they were formed. The next morning he suddenly had a dramatic episode of cyanosis and respiratory collapse. I have been thinking strongly in reading this history of the possibility that I just mentioned — injury to the adrenal glands. We know that the adrenal glands at birth are extremely vascular and highly friable. They are easily damaged and respond to infection in a dramatic way. They may become the site of massive hemorrhages, which manifest themselves with a picture of circulatory collapse, cyanosis, difficult breathing and distention of the abdomen. Hyperthermia and cutaneous hemorrhages may or may not be present. Certainly one should entertain that possibility, and I cannot erase it from my mind, even though I may be wrong in the last analysis.

There is another point of interest in that three hours before death bilateral swelling was noted in the mastoid region. At birth, pneumatization of the temporal bone has barely begun, there exists only one cell, — the mastoid antrum, — and the mastoid process is undeveloped. Development takes place some time later. The antrum is frequently the site of infection, especially following middle-ear infection, which in turn we can say is one of the most frequent findings in infants with acute nutritional disturbances. It sounds to me that this bilateral swelling might well have indicated subperiosteal abscesses in the regions of the antrums. That possibly ties up with the fact that we believe that the child had infection, which caused the vomiting and diarrhea, and that he possibly had a birth injury, and I daresay that possibly his death was due to massive adrenal hemorrhage.

DR ALLAN M BUTLER. I certainly agree with Dr Morelli regarding parenteral infection in a youngster like this. We have a clue to infection in the um-

bilicus, namely, the culturing of colon bacilli at three weeks of age. There are two questions concerning specific bits of information that I should like to ask. What did the urine show in terms of white cells and culture? What was the contaminant in the blood culture?

DR BENJAMIN CASTLEMAN The urine was not cultured. It was clear on admission, and the sediment contained 2 or 3 white cells and 2 or 3 epithelial cells per high-power field. The second specimen contained no cells. The blood culture contaminant was *Staph albus*, in one flask only.

DR BUTLER I was wondering if it was a colon bacillus, thinking of colon-bacillus septicemia, where so frequently there are hepatitis, pyelonephritis or infection elsewhere in youngsters of this age.

One might add that the bulging over the mastoid antrums previous to death brings up the whole question of the significance of such infections in many patients of this age group with nutritional disturbances. Way back in 1684 and again in 1920 a great deal of significance was attached to the organisms found at autopsy in such patients. This case received a lot of chemotherapy. It would, therefore, be interesting to know what the cultures from the middle ear and mastoid antrums showed. Such pus has been found to contain almost every variety of organism.

In obtaining the history it would have been important to check with the nursery from which this baby came to see if there was an epidermic diarrhea of the newborn or some such diarrhea as that described by Buddingh and Dodd.¹

DR CASTLEMAN The record states that the mother shared a room with someone else's baby who had the same symptoms.

DR GERTRUD REYERSBACH The hospital was called and denied that there had been any diarrhea.

CLINICAL DIAGNOSIS

Diarrhea
Bronchopneumonia?
Umbilical infection

DR MORELLI'S DIAGNOSES

Sepsis
Suppurative otitis media, involving both mastoid antrums
Hemorrhage into adrenal glands
Birth injury?

ANATOMICAL DIAGNOSES

Suppurative otitis media and mastoiditis, bilateral

Hemorrhage into adrenal glands, bilateral
Acute enteritis

PATHOLOGICAL DISCUSSION

DR CASTLEMAN At autopsy this baby's middle ears were filled with pus, which had extended into the mastoid antrums on both sides. We cultured the material on one side and recovered colon bacilli. I can find no note about what was recovered from the other side. We cultured colon bacilli from the pleural cavity. In the small and large intestines there were numerous ulcers, those in the large bowel being as large as 6 mm in length. They were fairly superficial, however, not extending deep into the mucosal layers. Cultures from these ulcers showed only colon bacilli. I do not believe that there is any question that the baby died of sepsis.

As Dr Morelli suggested, the adrenal glands were involved. The entire medulla of one was filled with blood. It had not enlarged the gland particularly, and was not a really big hematoma, but it probably was sufficient to account for the attack of collapse. The other adrenal gland had merely a few small hemorrhages, this was undoubtedly the same process to a lesser degree. I suppose it fits into the Waterhouse-Friderichsen syndrome, which can occur with any type of infection, not necessarily one caused by the meningococcus. The brain in this case was normal.

DR BUTLER Of course this youngster did not respond to intravenous glucose and saline as so many youngsters do who have adrenal difficulty underlying the clinical picture of collapse and dehydration.

As already indicated this case brings up the whole argument of the importance of considering antrotomy in patients with nutritional disturbances and some evidence of middle-ear infection. The argument often given by otolaryngologists is that one does not need to do an antrotomy because the communication between the antrum and middle ear is excellent. On the other hand, Marriott² used to say that the communication frequently was not free and that there was an accumulation of pus in the antrum that could not be relieved by opening the middle ear. Did you find as much pus in the middle ear as in the antrum? Was there any evidence of communication between the two?

DR CASTLEMAN We found pus in both antrums and middle ears, with good communications between them.

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CONGRATULATIONS TO THE HERALD

In an editorial in the June 24 issue of the *Boston Herald* attention was called to the danger of sensitization to the sulfonamides, even in small doses, when introduced into the body in various ways. It was further emphasized that dressings, ointments, powders and so forth containing such agents can still be bought without a prescription, except in New York City, where the Health Department has banned the indiscriminate sale of these products as well. The *Herald* conservatively states that the free sale of any sulfonamide "complicates practical therapeutics." The promiscuous use of such drugs has certainly created numerous and disabling complications, and the *Herald* is to be congratulated

for the emphasis to its readers of the risks of such medication.

This is an excellent example of the way in which the press can disseminate valuable medical information to the public. Possibly this comment was stimulated by a committee of the Massachusetts Medical Society. It is to be hoped so, for to gain the full support of the press in the release of medical facts and figures of value to the citizens of the community is one of the best means of educating the public regarding matters of this sort.

SEVERE PNEUMONITIS CAUSED BY A NEW PSITTACOSIS-LIKE VIRUS

A GREAT deal has been written in recent years about the so-called "virus pneumonias," but little is actually known concerning the etiology of the vast majority of these cases. Few if any of the several viruses that have recently been described have as yet proved to be of etiologic significance in more than an occasional case or a small group of cases. Thus, the virus of ornithosis has been recovered from only a few patients with pneumonia, and the development of antibodies against this agent has been demonstrated in only a few others. In most, if not all, such cases there was a history of reasonably definite exposure to infected birds. The condition is quite analogous in this respect to human infections with the closely related psittacosis virus. The rickettsia of Q fever has rarely been identified as the cause of pneumonia, the notable exception being an outbreak that occurred among the workers at the National Institute of Health.¹ In that outbreak the mode of infection was not definitely established, since those who were afflicted had not been directly exposed to the agent. The rickettsias were being cultured in the laboratory, however, and the pathogenicity of the agent and its mode of spread are such as to make an occurrence of this sort quite possible. None of these agents have proved to be the cause of the large number of cases of primary atypical pneumonias that have been encountered in both the military and civilian populations of this country. Furthermore, the etiologic significance of all the other agents that have been described has not been confirmed.

A recent outbreak of severe pneumonitis in Louisiana²⁻⁵ is of interest because of the finding of a new virus transmissible to animals and apparently spread by contact with infected patients. The epidemic occurred in six isolated communities in the bayou region of Louisiana, the cases being scattered over an area of approximately 20,000 square miles. The disease was recognized as an entity only after an epidemiologic study of 3 cases had been undertaken. It was unusual in that it spread only among nursing contacts and had a high mortality, there being 8 deaths among the 19 recognized cases.

The first case was that of the wife of a trapper, who developed a febrile illness on December 2, 1942, she became progressively worse and was transferred to a sanatorium about 120 miles from her home, where she died on December 18. A nurse who attended this patient and her husband, who likewise helped care for her, both became ill on December 24. The nurse was treated at the sanatorium, where she died on January 6. Before that time, however, she was the source of 6 other cases in nurses and in persons who acted as nurses. The husband became ill after returning home and died on December 26. Of the secondary cases, only the fatal ones spread the disease, and the same was true of subsequent cases. Rigorous control measures were instituted, and after that time, except for an attendant who developed the disease while she was still in quarantine, no further spread occurred. It is of interest that the fatal cases were contagious only during the last forty-eight hours of their disease.

The incubation period was estimated as being between six and nineteen days. Transmission was only through direct contact with cases; no evidence could be found of living or intermediate vector, nor were human carriers or mild cases discovered. There were many possibilities of animal reservoirs, but few of these were adequately explored.

In the course of the epidemiologic studies it was discovered that a similar epidemic had occurred in March, 1936. The clinical picture, as described by the physician who attended the cases, was quite similar. In addition, secondary cases occurred only in the nursing contacts of the fatal cases and there were 5 deaths among the 7 secondary cases that were traced.

The clinical features were characteristic in all cases. The onset was mild, with headache and backache followed by slight chills, sweating and a concurrent abrupt rise in temperature. Pneumonitis was demonstrated early by physical and x-ray examinations. In spite of that fact the patients presented the appearance of well-being throughout the first week and into the second week of their illness and then abruptly went into a state of collapse. This was often accompanied by delirium and cyanosis, and the syndrome sometimes recurred at intervals until recovery or death. The white-cell count was low or normal, only occasionally being slightly elevated. Death usually occurred between the seventh and fifteenth days, and in one case on the thirty-ninth day. The febrile course in those who recovered lasted from two to five weeks. Convalescence in all cases was prolonged, several months usually being required before normal health was restored. Transient alopecia occurred in 3 patients.

Autopsies in 2 fatal cases showed similar changes in each. The lungs revealed sharply defined areas of plum-colored consolidation, an alveolar exudate chiefly composed of large mononuclear cells, hyperplasia of the alveolar lining cells and slight or no involvement of the bronchioles or bronchi. No significant bacteria were found, but a few clusters of minute, basophilic, coccobacillary, cytoplasmic inclusions were seen in the pulmonary alveoli, as well as in the Kupffer cells in one of the cases. The anatomical findings resembled those of psittacosis but showed little in common with those of Q fever.

A virus was obtained from throat washings in 3 of the 4 cases that were tested, and in 2 fatal cases it was also isolated from autopsy material. It was propagated in white mice by either intraperitoneal or intranasal inoculation and in guinea pigs by intraperitoneal inoculation, using either the throat washings or tissue suspensions. The symptoms and gross lesions in animals were similar to those observed with the psittacosis group of viruses, and there were readily demonstrable elementary bodies in stained smears of the spleen, liver and lungs of the infected animals. Guinea pigs respond with a fatal infection, and mice succumb when they are inoculated by any of the usually used routes, that is, intranasally, intraperitoneally, intracerebrally, intramuscularly

or subcutaneously No other known virus exhibits a similar pathogenicity, and for this reason the virus is probably new

The possible origin of this new virus in the wild life of the bayou region, its apparent relation to other psittacosis-like viruses, the severity of the disease and the viral spread by contact from fatal cases signify that the virus is an important infective agent. Furthermore, the pathogenicity of the virus for laboratory animals appears to be such as to make it easily recognizable should it be looked for in the future

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MASSACHUSETTS MEDICAL SOCIETY

POSTWAR PLANNING COMMITTEE

The value of co-operation between physicians, hospital executives and hospital trustees was emphasized at a meeting called by the Postwar Planning Committee on June 20 Representatives of the ninety-eight hospitals in Massachusetts having a capacity of 100 beds or more, including the trustees, the superintendents and the chiefs of the medical and surgical services, met at the invitation of the committee to discuss various aspects of the problems involved in providing adequate opportunities for the postgraduate training of doctors returning from the service at the end of the war, for the extension of postgraduate instruction to all doctors in Massachusetts and for the promotion of health education among the laity Stimulating suggestions were made by various speakers, one suggesting that a trustee of a large metropolitan hospital, by serving also as a trustee in a hospital at a distance, might bring about an exchange of ideas that would be of benefit to both institutions It was pointed out that an increase in the number of residencies would also improve the care given to hospital patients

Among the guests of the committee were nine members of the Massachusetts General Court, who, by their presence, evidenced the increasing interest of legislative representatives in the progressive activities of the Society

It is to be hoped that this meeting will be followed during the next two or three months by similar meetings in various communities of the Commonwealth

HOWARD F ROOT, *Chairman*

DEATH

HAMMOND — William J Hammond, M D, of East Walpole, died July 4 He was in his seventy-seventh year Dr Hammond received his degree from Harvard Medical School in 1899 He was a member of the American Psychiatric Association, the New England Society of Psychiatry, and the Association for Research in Nervous and Mental Diseases and a fellow of the American Medical Association His widow survives

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

HILDRETH — Lewis G Hildreth, M D, of Marlboro, died June 25 He was in his seventy-eighth year Dr Hildreth received his degree from the Kentucky School of Medicine in 1892 His widow, a daughter and four sons survive

MISCELLANY

ALVARENGA PRIZE TO DR WIENER

In recognition of his important work on the various Rh blood factors and on their genetic transmission, the College of Physicians of Philadelphia, on July 14, awarded the Alvarenga Prize to Alexander S Wiener Dr Wiener will give the Alvarenga Lecture before the College of Physicians of Philadelphia and the Philadelphia County Medical Society on October 3, the title being "Rh Blood Factors in Clinical Medicine"

The Alvarenga Prize was established by the will of Pedro Francisco da Costa Alvarenga, of Lisbon, Portugal, an associate fellow of the College of Physicians, "to be awarded annually by the College of Physicians on each anniversary of the death of the testator, July 14, 1883" The College usually makes this award for outstanding published work, inviting the recipient to deliver the Alvarenga Lecture

CORRESPONDENCE

MAX MEYERHOF

To the Editor Word has come from Mizraim An old doctor died in Cairo, and funeral services were held for him in the Ashkenazi Synagogue on April 23 He was an eye specialist, who also wrote several books on the scientific heritage of the Arabs, according to the obituary column in the *New York Times* For further identification of the dead, it was mentioned by the newspaper that he was the cousin of a physiologist who had won the Nobel Prize in 1922 Ten short lines, fifty words in all, at the tail end of a narrow column, to summarize the achievements of a long life of scientific research!

Max Meyerhof originated from a family of distinguished scientists and physicians His maternal uncle was practicing gynecology in Breslau when he was born in Hildesheim on March 21, 1874 Perhaps the memory of his uncle moved him to take up medicine as a profession He studied at Hannover, Heidelberg, Berlin and Strassburg, where he graduated in 1897 Bacteriology was then a novelty, and young Dr Meyerhof spent a year (1898) as assistant bacteriologist in the Public Health Institute of Strassburg, studying the biology of the diphtheria bacillus and the mysteries of *Proteus vulgaris*

This year also brought him closer to his young relative Wilhelm Spiegelberg, professor of Egyptology at Strassburg University The lectures of his cousin awoke in him a long-

ing for the land of ancient culture and hieroglyphs. This longing was stimulated further by his postgraduate studies in ophthalmology (1899), at the Berlin and Breslau eye clinics he learned that Egypt is rich not only in hieroglyphs but also in eye diseases. After a preliminary trip to the land of pyramids in 1900, he decided to emigrate from Germany.

In 1903 Meyerhof arrived at Cairo and began his ophthalmologic practice. The next year he was already a member of the Ophthalmological Society of Egypt. Since Cairo is a city of many nations and many languages, where a successful medical practice requires a real linguist, Meyerhof devoted several years to learning Hebrew, Arabic, Persian, Syriac, Turkish and other Oriental languages. These studies brought him closer not only to his patients but also to his colleagues and to the scholars of his adopted land. And the metamorphosis began—Meyerhof, the ophthalmologist, developed into Meyerhof, the medical historian.

During the period of his first stay in Egypt (1903-1914) he was chiefly the eye specialist, the medical practitioner, whose observations and essays filled many pages in the bulletins of his society. He found a veritable museum of eye diseases in his office: purulent conjunctivitis, corneal granulations of all types, eyes affected by leprosy, vernal conjunctivitis, tumors of the eyelids, all types of foreign bodies. He investigated all stages of trachoma, the causes of the disease and its immunological peculiarities, and his interest in this subject remained alive even in his later years.

For his ophthalmologic research he was honored by his Egyptian colleagues, who, in 1909, elected him, the thirty-five-year-old foreigner, to the presidency of the Ophthalmological Society. In this office he showed himself a real benefactor of Egypt by organizing a nation-wide service for the treatment of eye diseases and by establishing an ophthalmologic department at the King's Hospital in 1910.

His frequent visits to the libraries of Cairo, and the stimulating contact with such friends as the scholarly Ahmad Taimur Pasha, led him toward a new field of activity—medical history in general, and the history of ophthalmology in particular. His first medicohistorical study appeared in the 1906-1907 volume of an ophthalmologic journal, and was soon followed by others. He fell in love with Clio, and with the ancient Arabic manuscripts in the Library of the Khedive and in the private collections of Egyptian noblemen. Then, World War I ended his happiness for a period.

His forced volunteering as a physician in the German army resulted in a waste of ten years (1914-1923). After the war, he had to stay in Hannover, where, engaged in medical practice, he waited for a change in the political atmosphere of Europe. In 1923 he was allowed to return to Egypt, only to find part of his library dissipated and some of his notes lost. But he started all over again, this time as Meyerhof, the Arabic scholar and historian. A series of journal articles and books, all of them based on painstaking investigations, is the result of this second period of his productive life.

In 1926 he found the Syriac and Arabic translations of certain treatises of Galen, treatises lost for us, both in the original Greek and in the Latin version. He also showed us the importance of Arab culture in every branch of modern science in the book *Le monde islamique* (Paris, 1926). Two years later, on its centennial celebration, the Egyptian University published his main work, a critical edition of *Ten Treatises on the Eye* (Kitab al-ashr maqalat fi'l-ain), ascribed to Hunain ibn-Ishaq (809-877). By editing the Arabic text with a translation of this rare manuscript, Meyerhof's contribution to science was invaluable, since Hunain's work is not only the earliest existing textbook on the eye and its diseases, but also the starting point of Arabic ophthalmology. For it he justly received an honorary Ph.D. degree from the University of Bonn and an honorary membership in the Royal Society of Medicine in London.

There are many more manuscripts in the old libraries, and from 1928 to 1938 we became acquainted with the work of many other early Arab and Persian physicians, through the researches of Meyerhof in the *Paradise of Wisdom of Ali at-Tabari* (Iss, 1921), the ophthalmologic *Al-murshid fi'l-kohl of ibn-Aslam al-Gafiqi* (Masnou, 1933), the abridged version of the *Book of Simples of ibn-Muhammad al-Gahqi* (Cairo, 1933-1940) and the pharmacologic work of Beruni (1933). His most widely appreciated finding (1933) is, however, the work of the thirteenth-century ibn-an-Nafis, whom he proved to be the real discoverer of the pulmonary circulation of blood.

The last few years of his life were again disturbed by another world war, and the persecution of his race. His interest turned to Jewish affairs, to the medieval Jewish physicians in the Near East and to that great Jew of the twelfth century, the second Moses, whose life ended in Cairo, Moses ben Maimon. His Maimonides studies are now left unfinished. Death also spoiled the great ambition of his life—to find the lost manuscript of the admirable work of ibn al-Haitham on the optics and vision.

In his adopted land he will be remembered as the German doctor who pitied the poor fellahs, with their bloodshot, discharging and blind eyes, as the great humanitarian who organized medical care for a plagued nation's relief. His many friends in the world will soon feel the loss of the foremost historian of medieval Arab medicine, who for many years kept the door of Eastern wisdom open for Western science. With his broad medical background, linguistic knowledge, and love of old moldy manuscripts, he represents to me the ideal medical historian, whose empty home in Cairo now turns into the lost Kaaba of many a planned pilgrimage.

CLAUDIUS F. MAYER, M.D.

Army Medical Library
Washington, D. C.

USE OF THE WORD "ANTIBIOTIC"

To the Editor: It has now been about three years since the terms "antibiotic" and "antibiotic effect" were suggested by Waksman, Horning, and Spencer. The fact that these expressions have gained wide acceptance in a short time shows that they have answered a real need for such terms. There are, however, good reasons for questioning the propriety of limiting the application of so broad and useful a word as "antibiotics" to one particular category of substances that are destructive to life. Certainly many products of the manufacturing chemist, such as the arsenicals, the mercurials, and many different types of radiant energy are true antibiotics. The agents that are now being obtained from various forms of bacteria and lower fungi might be referred to simply as bacterial or fungous antibiotics, or from a semantic standpoint the word "mycoantibiotics" has much to commend it. In any event, I venture to suggest that the field of usefulness of the word "antibiotics" should not be circumscribed by conventionally limiting its application to one group of substances alone, especially when from an etymologic viewpoint such restricted use of the term hardly seems justified. Should the word come to be used in a more general sense than being confined to the "mycoantibiotics," then other similar expressions, such as "chemoantibiotics" and "actinoantibiotics," would probably come into use as special group terms.

SURGEON M. WINGO, M.D.

United States Coast Guard Academy
New London, Connecticut

BOOK REVIEW

Gynecological and Obstetrical Urology. By Houston S. Everett, M.D. 8th, cloth, 517 pp., with 220 illustrations. Baltimore: Williams and Wilkins Company, 1944. \$6.00.

The twenty-three chapters that make up this book offer its readers a review of urology. Anatomy, physiology, diagnosis and treatment are discussed from the experiences of the Gynecological Department of the Johns Hopkins Hospital and University.

It is questionable whether a book of this size can adequately cover the entire field of urology, even when limited to the female patient. Gynecology and urology meet in many conditions, such as urinary fistulas, tumors of the urethra, inflammatory changes and cancer. This common ground is important to both specialists and deserves more consideration than this book provides, since so much space is devoted to urology alone. Much more could have been written on the management of urinary-tract complications that follow operation and on irradiation of the female genital tract.

The author is an enthusiastic follower of the teachings of Hunner, many of whose principles have not been accepted by the average urologist. Those who believe with Hunner, however, will read this book with great satisfaction.

(Notices on page xvii)

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THE SURGICAL TREATMENT OF CARCINOMA OF THE RECTUM*

Statistics on 198 Cases of Resection

E. PARKER HAYDEN, M.D.†

BOSTON

CARCINOMA of the rectum and sigmoid is often encountered and is much more frequent in that segment than in other parts of the colon. It seems unnecessary to discuss the symptoms of this disease or to advance any arguments in favor of surgical treatment as against radiotherapy. It is doubtless generally agreed that radical surgery should be carried out whenever possible. In the presence of one or two metastases in the liver, or when the local growth, although extensive and perhaps abscessed, can still be removed, I have always completed the operation if possible, being willing to accept a higher mortality rate for the sake of giving relief, if not cure, in this unfavorable group of cases. Thus it is that of 217 patients explored, in only 19 was the carcinoma found to be so extensive as to make a radical procedure foolhardy, whereas in 198 the growth was removed by one of the several types of radical operation (Table 1). The evolution of operative procedures, from the limited posterior excisions of the 1880's and 1890's

None of these methods permit so thorough a removal of mesentery as does abdominoperineal resection, yet surgeons do use all of them and obtain cures. Their relative frequency in my experience is shown in Table 2. The safety of a single-stage

TABLE 2 *Methods of Resection*

TYPE OF OPERATION	No. of Cases
Abdominoperineal resection	
One stage	131
Two-stage	27
Anterior resection	16
Mikulicz resection	10
End to-end suture	13
Tube resection	1
Total	198

abdominoperineal resection, with adequate pre-operative preparation, is such that I now rarely resort to a two-stage procedure, other than an occasional cecostomy as a preliminary decompression for marked obstruction.

The two-stage procedures, used in 27 cases, consisted of three methods: colostomy followed by posterior resection, the Jones operation, in which the colon is not divided at the first stage but is brought out as a loop colostomy after dissection of the pelvis, and the Lahey procedure, in which the sigmoid loop and mesentery are divided and separated at the first operation, both bowel ends being brought out through the abdominal wall. Dr. D. F. Jones often emphasized the risks involved, after dividing a sigmoid, in placing the inverted and devitalized lower segment below the peritoneum and leaving it there a week or more before doing the perineal part of the operation. On two occasions, when I had planned a one-stage operation, the patient's condition at the end of the abdominal part of the procedure was such that I decided against perineal removal at that time, doing it two days later without any unusual sepsis or other complications. To have left the lower segment, with its reduced blood supply, in the hollow of the sacrum longer than forty-eight

TABLE 1 *Operability*

PROCEDURE	No. of Cases
Operation not advised	7
Operation advised but refused	14
Case considered inoperable	19
Radical resection	198
Total	238

to the present widely used abdominoperineal resection, has been based on a sound conception of what constitutes the most thorough removal of gland-bearing areas and primary lesions. Every surgeon is occasionally tempted to do something less than this, if the tumor is high enough in the sigmoid to permit either a resection with permanent colostomy and inversion of a short rectal stump, a Mikulicz resection or a resection with end-to-end suture

*Presented at the annual meeting of the New England Surgical Society, Boston, September 20, 1944.

†Associate visiting surgeon, Massachusetts General Hospital.

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His frequent visits to the libraries of Cairo, and the stimulating contact with such friends as the scholarly Ahmad Taimur Pasha, led him toward a new field of activity—medical history in general, and the history of ophthalmology in particular. His first medicohistorical study appeared in the 1906–1907 volume of an ophthalmologic journal, and was soon followed by others. He fell in love with Clio, and with the ancient Arabic manuscripts in the Library of the Khedive and in the private collections of Egyptian noblemen. Then, World War I ended his happiness for a period.

His forced volunteering as a physician in the German army resulted in a waste of ten years (1914–1923). After the war, he had to stay in Hannover, where, engaged in medical practice, he waited for a change in the political atmosphere of Europe. In 1923 he was allowed to return to Egypt, only to find part of his library dissipated and some of his notes lost. But he started all over again, this time as Meyerhof, the Arabic scholar and historian. A series of journal articles and books, all of them based on painstaking investigations, is the result of this second period of his productive life.

In 1926 he found the Syriac and Arabic translations of certain treatises of Galen, treatises lost for us, both in the original Greek and in the Latin version. He also showed us the importance of Arab culture in every branch of modern science in the book *Le monde islamique* (Paris, 1926). Two years later, on its centennial celebration, the Egyptian University published his main work, a critical edition of *Ten Treatises on the Eye* (Kitab al-ashr maqalat fi'l-ain), ascribed to Hunain ibn-Ishaq (809–877). By editing the Arabic text with a translation of this rare manuscript, Meyerhof's contribution to science was invaluable, since Hunain's work is not only the earliest existing textbook on the eye and its diseases, but also the starting point of Arabic ophthalmology. For it he justly received an honorary Ph.D. degree from the University of Bonn and an honorary membership in the Royal Society of Medicine in London.

There are many more manuscripts in the old libraries, and from 1928 to 1938 we became acquainted with the work of many other early Arab and Persian physicians, through the researches of Meyerhof. The *Paradise of Wisdom* of Ali at-Tabari (Istisr, 1921), the ophthalmologic *Al-murshid fi'l-kohl* of Ibn-Aslam al-Gafiqi (Masnou, 1933), the abridged version of the *Book of Simples* of Ibn-Muhammad al-Gafiqi (Cairo, 1933–1940) and the pharmacologic work of Beruni (1933). His most widely appreciated finding (1933) is, however, the work of the thirteenth-century Ibn-an-Nafis, whom he proved to be the real discoverer of the pulmonary circulation of blood.

The last few years of his life were again disturbed by another world war, and the persecution of his race. His interest turned to Jewish affairs, to the medieval Jewish physicians in the Near East and to that great Jew of the twelfth century, the second Moses, whose life ended in Cairo, Moses ben Maimon. His Maimonides studies are now left unfinished. Death also spoiled the great ambition of his life—to find the lost manuscript of the admirable work of Ibn al-Haitham on the optics and vision.

In his adopted land he will be remembered as the German doctor who pitied the poor fellahs, with their bloodshot discharging and blind eyes, as the great humanitarian who organized medical care for a plagued nation's relief. Hu many friends in the world will soon feel the loss of the foremost historian of medieval Arab medicine, who for many years kept the door of Eastern wisdom open for Western science. With his broad medical background, linguistic knowledge, and love of old moldy manuscripts, he represents to me the ideal medical historian, whose empty home in Cairo now turns into the lost Kaaba of many a planned pilgrimage.

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USE OF THE WORD "ANTIBIOTIC"

To the Editor: It has now been about three years since the terms "antibiotic" and "antibiotic effect" were suggested by Waksman, Horning, and Spencer. The fact that these expressions have gained wide acceptance in a short time shows that they have answered a real need for such terms. There are, however, good reasons for questioning the propriety of limiting the application of so broad and useful a word as "antibiotics" to one particular category of substances that are destructive to life. Certainly many products of the manufacturing chemist, such as the arsenicals, the mercurials, and many different types of radiant energy are true antibiotics. The agents that are now being obtained from various forms of bacteria and lower fungi might be referred to simply as bacterial or fungous antibiotics, or from a semantic standpoint the word "mycoantibiotics" has much to commend it. In any event, I venture to suggest that the field of usefulness of the word "antibiotics" should not be circumscribed by conventionally limiting its application to one group of substances alone, especially when from an etymologic viewpoint such restricted use of the term hardly seems justified. Should the word come to be used in a more general sense than being confined to the "mycoantibiotics," then other similar expressions, such as "chemoantibiotics" and "actinoantibiotics," would probably come into use as special group terms.

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BOOK REVIEW

Gynecological and Obstetrical Urology. By Houston S. Everett, M.D. 8°, cloth, 517 pp., with 220 illustrations. Baltimore: Williams and Wilkins Company, 1944. \$6.00.

The twenty-three chapters that make up this book offer its readers a review of urology. Anatomy, physiology, diagnosis and treatment are discussed from the experiences of the Gynecological Department of the Johns Hopkins Hospital and University.

It is questionable whether a book of this size can adequately cover the entire field of urology, even when limited to the female patient. Gynecology and urology meet in many conditions, such as urinary fistulas, tumors of the urethra, inflammatory changes and cancer. This common ground is important to both specialists and deserves more consideration than this book provides, since so much space is devoted to urology alone. Much more could have been written on the management of urinary-tract complications that follow operation and on irradiation of the female genital tract. The author is an enthusiastic follower of the teachings of Hunner, many of whose principles have not been accepted by the average urologist. Those who believe with Hunner, however, will read this book with great satisfaction.

(Notices on page xvii)

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THE SURGICAL TREATMENT OF CARCINOMA OF THE RECTUM*

Statistics on 198 Cases of Resection

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BOSTON

CARCINOMA of the rectum and sigmoid is often encountered and is much more frequent in that segment than in other parts of the colon. It seems unnecessary to discuss the symptoms of the disease or to advance any arguments in favor of surgical treatment as against radiotherapy. It is doubtless generally agreed that radical surgery should be carried out whenever possible. In the absence of one or two metastases in the liver, or when the local growth, although extensive and perhaps abscessed, can still be removed, I have always completed the operation if possible, being willing to accept a higher mortality rate for the sake of giving relief, if not cure, in this unfavorable group of cases. Thus it is that of 217 patients explored, in only 19 was the carcinoma found to be so extensive as to make a radical procedure foolhardy, whereas in 198 the growth was removed by one of the several types of radical operation (Table 1). The evolution of operative procedures, from the limited posterior excisions of the 1880's and 1890's

None of these methods permit so thorough a removal of mesentery as does abdominoperineal resection, yet surgeons do use all of them and obtain cures. Their relative frequency in my experience is shown in Table 2. The safety of a single-stage

TABLE 2 *Methods of Resection*

TYPE OF OPERATION	NO OF CASES
Abdominoperineal resection	
One-stage	151
Two-stage	27
Anterior resection	16
Mikulicz resection	10
End-to-end suture	15
Tube resection	1
Total	198

abdominoperineal resection, with adequate pre-operative preparation, is such that I now rarely resort to a two-stage procedure, other than an occasional cecostomy as a preliminary decompression for marked obstruction.

The two-stage procedures, used in 27 cases, consisted of three methods: colostomy followed by posterior resection, the Jones operation, in which the colon is not divided at the first stage but is brought out as a loop colostomy after dissection of the pelvis, and the Lahey procedure, in which the sigmoid loop and mesentery are divided and separated at the first operation, both bowel ends being brought out through the abdominal wall. Dr D F Jones often emphasized the risks involved, after dividing a sigmoid, in placing the inverted and devitalized lower segment below the peritoneum and leaving it there a week or more before doing the perineal part of the operation. On two occasions, when I had planned a one-stage operation, the patient's condition at the end of the abdominal part of the procedure was such that I decided against perineal removal at that time, doing it two days later without any unusual sepsis or other complications. To have left the lower segment, with its reduced blood supply, in the hollow of the sacrum longer than forty-eight

TABLE 1 *Operability*

PROCEDURE	NO OF CASES
Operation not advised	7
Operation advised but refused	14
Case considered inoperable	19
Radical resection	198
Total	238

to the present widely used abdominoperineal resection, has been based on a sound conception of what constitutes the most thorough removal of gland-bearing areas and primary lesions. Every surgeon is occasionally tempted to do something less than this, if the tumor is high enough in the sigmoid to permit either a resection with permanent colostomy and inversion of a short rectal stump, a Mikulicz resection or a resection with end-to-end suture

*Presented at the annual meeting of the New England Surgical Society, Boston, September 20, 1944.

†Associate visiting surgeon, Massachusetts General Hospital.

hours would have invited infection, which might well have been serious or fatal. Only rarely should it be necessary to divide the operation in this way, but it can be done in an emergency.

Anterior resection may be used to avoid a perineal extraction if the tumor is too low for a safe anastomosis or a Mikulicz operation but high enough to permit division of the bowel below it with a fair margin and a satisfactory inversion of the rectal stump above the peritoneal level. To leave the stump below the peritoneum invites retroperitoneal infection, which may well be serious. This is an operation that I have not found to be satisfactory and that I rarely perform.

End-to-end suture can be done when a tumor is a little higher than just mentioned but not high enough for a Mikulicz operation, which requires a rather long lower segment below as well as above the tumor.

Tube resection, for a tumor too low for anterior resection, and when preservation of an anal outlet seems necessary, is an operation rarely indicated.

Abdominoperineal resection in one stage is the ideal procedure for carcinoma of the rectum and sigmoid, and offers the highest hope of a cure. I have rarely been compelled to abandon plans for this procedure because of a patient's refusal to have a colostomy. I have always thrashed out this question in advance with the patient, although not always saying flatfootedly that it would have to be done without question.

A stay of three to five days in the hospital before operation on the colon is usually an adequate period for general rest, preparation of the bowel, completion of laboratory work and whatever measures seem necessary to improve the patient as an operative risk.

Unless contraindicated I have used pontocaine spinal anesthesia, which greatly facilitates the ease of operation, as contrasted with the more difficult relaxation under ether. A moderate Trendelenburg position is sufficient, although a high one is better. The patient is sometimes bothered by too high an inversion.

I have usually placed the colostomy in the long left paramedian incision, without suture of the left lateral gutter, since there is about as much room for small bowel on the left as on the right side of the suspended colon. If the descending colon is brought out through a lateral rectus stab wound, the smaller lateral aperture should be closed, since there is much greater likelihood of small-bowel herniation with obstruction through a small aperture.

The perineal part of the operation I have carried out with the patient in the right Sims position. After removal of the bowel segment the posterior wound is packed with a large gauze handkerchief inside of a rubber dam, and the wound is sutured from its upper end down to the drain, which comes out anteriorly.

The colostomy is opened in twenty-four or forty-eight hours, an enema given on the fourth or fifth day, and boric irrigations of the posterior wound are begun after removal of the posterior pack at about the same time and continued until the discharge ceases.

The average postoperative hospital stay is three weeks.

In several cases I have removed the uterus and adnexa with the bowel segment, and occasionally part or all of the posterior vaginal wall. Resection of a loop of small bowel that has become involved in tumor by adherence to the main growth, with anastomosis of the ends, is sometimes necessary.

Of the resections in this series of 198 cases, 131 were performed over three years ago and 98 over five years ago, the remaining 60 have been done more recently and therefore have no end-result value. In every case where it was possible to do so, as previously stated, the growth was removed even if the outlook for cure was not good, and regardless of the age of the patient, if there seemed a reasonable likelihood of his surviving the operation.

In the entire series there were 26 hospital deaths, a mortality of 13 per cent, with autopsies in 11 cases. The chief causes of death are given in Table 3.

TABLE 3 Causes of Death in Hospital

CAUSE OF DEATH	No OF CASES
Pneumonia	8
Septis	7
Embolus	3
Obstruction	2
Shock	1
Anesthesia	1
Uremia	1
Coronary occlusion	1
Cardiac decompensation	1
Suicide	1
Total	26

These patients varied in age from twenty-seven to seventy-five, but 22 were over fifty-four.

The operations performed in these fatal cases are shown in Table 4. Although over 50 per cent of the deaths occurred in cases receiving one-stage resection, this should not be considered an indictment of the procedure, since actually the 14 deaths were only 10 per cent of the 131 single-stage resections—a mortality lower than that of the series as a whole.

TABLE 4 Operations Performed in Fatal Cases

TYPE OF OPERATION	No OF CASES
Abdominoperineal resection	14
One stage	2
Two-stage	2
Anterior resection	4
Mikulicz resection	2
End-to-end suture	3
Tube resection	1
Total	26

The deaths from embolism occurred in 3 cases in which operation was done in the present era.

of femoral-vein ligations It is of interest that thrombosis of one or both iliac arteries and their tributaries was found at autopsy in 2 of these, whereas in the third the pathologist could not determine the origin of the embolus

Of the 198 patients resected, 75 died later, in most cases of recurrent disease, 12 of these died of unrelated causes, and 96 are still alive Of the 98 patients operated on over five years ago, 32, or 33 per cent, have survived without evidence of disease for five to fourteen years (Table 5) The latest

TABLE 5 Radical Resections Performed Over Five Years Ago

RESULT	NO OF CASES	PERCENTAGE
Died in hospital	12	12
Died later	54	55
Alive and well	32	33
Total	98	

death from recurrent disease occurred five years and five months after operation

In general, the patients who died later of recurrence were the ones whose tumors were classified as Grade II or III adenocarcinoma, who had metastases in the lymph nodes at operation or who had a long history of symptoms and a large tumor invading the serosa and extending beyond it There were, however, exceptions to this Likewise, in the group of cured cases, were some with lymph-node involvement and a large tumor

SUMMARY

The surgical treatment of 198 cases of carcinoma of the rectum in which radical resection was performed is discussed A five-year cure rate of 33 per cent was obtained

A single-stage abdominoperineal resection is recommended, the operative mortality in such cases having been 10 per cent, compared with an over-all mortality of 13 per cent

DISCUSSION

DR FRANK H LAHEY, Boston I must say something about cancer of the rectum because of our large experience with it This is a fine series, and Dr Hayden is to be complimented It represents the standard of the country for carcinoma of the rectum as to operability, mortality and general results, and I do not believe that it could have been improved on materially Cancer of the rectum is still a field that can be improved, however, in terms of approach from the standpoint of the general practitioner and the public

Before I report our end results I should like everyone to recall a few things that we are not doing in cases of cancer of the rectum For one, we are not educating the general practitioners and the public enough to the fact that diagnosis does not have to be made solely by digital examination and does not have to be made by roentgenogram, but is to be found in the history in nearly all the cases Dr Swinton, in our clinic — I have repeated this statement a hundred times, but it contains such a lesson that I continue to do so, — studied 100 proved cases of carcinoma of the right colon, 100 proved cases affecting the left colon and 100 proved cases involving the rectum, and in reviewing the histories asked question, Was there blood in the stool, alter-

ation in bowel function or pain of an obstructive character? In these cases the answer was "yes" in nearly 98 per cent, in other words, the diagnosis could have been made almost by mail

We need to educate the lay public more along these lines About 3 out of every 100 persons have polyps of the large bowel and rectum We must approach cancer of the rectum and colon in the precancerous stage, and include in our procedures proctoscopic and sigmoidoscopic examinations and contrast enemas In many of these cases, a history can be obtained of blood in the stools long before carcinoma could have been present, indicating that the lesion was at first a polyp

I dislike to present our figures because they are always so large Nevertheless, I have to present them to you because it is from them that we must draw our conclusions

We have operated on 1800 patients for carcinoma of the colon and rectum, of whom 1200 or 1300 had carcinoma of the rectum and 500 or 600 had carcinoma of the colon It is interesting that the operative mortality was originally 103 per cent In the last five years for the whole group it has dropped to 50 per cent In the last two years the mortality in cases of carcinoma of the colon has dropped to 28 per cent, and that in cases of carcinoma of the rectum to 39 per cent

Our operability is much the same as Dr Hayden's, 85.5 per cent It is also interesting to realize that 9.6 per cent of the patients in whom we resected the rectum had metastases to the liver, and in about 22 per cent of the cases there was involvement of other structures, such as neighboring segments of bowel, the uterus, the bladder or some other structure In at least 60 cases we have removed the rectum, uterus, tubes, ovaries and part of the vagina If the whole series of patients is put together, including those in which other organs were involved and those with metastases to the liver, 53 per cent of them are alive and well after five years without evidence of recurrence It is important to remember that this series includes palliative operations, so that the over-all figure for the cases that were operable is higher

We have done two-stage resections of the type that I have described in about 400 cases We now do one-stage operations in about 81 per cent I agree with Dr Hayden that if one can see the pathological report, one can tell from this large experience about what will happen to these patients If there is no lymph-node or blood-vessel involvement and the lesion is limited to the section of bowel removed, 90 per cent of the patients will be alive and well for over five years without evidence of recurrence These are the favorable cases If there are lymph-node metastases, only 37 per cent will be alive and well without recurrence, and if there is involvement of other structures, such as neighboring sections of bowel, 30 per cent will be alive and well Unfortunately, if there is blood-vessel invasion the one thing that means recurrence only 14 per cent will survive for over five years

There is a school of thought in the country today, based on sentiment concerning the sphincter, that advocates limited procedures I have read and heard several papers on preservation of the sphincter and formation of perineal colostomies, and I believe that these are bad When one tries to accomplish two things one loses something in each — one cannot have one's cake and eat it, too, when one approaches the question of cancer I do not care how small the lesion is, if it is truly carcinoma, the resection should be all the more aggressive, because thus there is a better opportunity to cure these patients at that time When one tries to preserve the colon in terms of getting it down to the perineum, one unconsciously limits the radicalness of the procedure After all, who wants a colostomy in the perineum, where the only way one can see it is with a mirror? I should much rather have one where it can be taken care of, and it can now be well handled with all the plans we know for managing colostomies We sell no bags None of our patients wear bags They can be trained so to constipate themselves and substitute irrigation for defecation that they do not need bags Therefore I do not see any reason why we should do anything that can limit the radicalness of procedures for the removal of such tumors

In regard to colostomies, do not let these patients get away from your oversight for the first six months They lose their morale during that time and that is the time that they have to be educated regarding the colostomy There

must be someone to whom they can write or talk about their problems. Another thing is to teach them to establish what their bowel habits are to be, in terms of irrigation every two or three days. When these habits are established, they can do almost anything that they have done previous to the institution of the colostomy.

I think that colostomy has such a bad name because the palliative type, with a living death attached to it, is largely the only one about which people and physicians know. When more patients and physicians are familiar with the colostomy after the lesion is removed, they will realize that it is entirely different from the one in which the lesion is still present, causing most of the symptoms associated with palliative colostomy.

This is still a great field for advancement, and the paper of Dr. Hayden presents an admirable personal series, with fine end-results.

DR. DAVID CHEEVER, Boston. There are many here better qualified to discuss this subject than I, and I have little to say. I heard some of Dr. Hayden's paper and thought it excellent, and based on an extremely good record of personal results. I agree entirely with Dr. Hayden and Dr. Lahey about the necessity of educating the public about colostomy.

It is very interesting for the older men to think back over the general course of events in the history of the operation for carcinoma of the rectum—that is, to go back to the older days when, as I well remember, Dr. Maurice Richardson used to say, "If I had carcinoma of the rectum, I should go to the poorest surgeon I could find and ask him to do the most extensive operation he could do." The inference is obvious.

The greatest advance that has been made in one sense in the treatment of carcinoma of the rectum is the recognition, as Dr. Lahey says, that the perineum is the very worst place to have a postoperative opening, and that we are striving for an impossible ideal in making the anus where Nature placed it first. This was for years and years one of the greatest mistakes that we could have made, and it was only when we made up our minds that we should not strive for an impossible and impracticable ideal that we made further progress.

I also agree keenly with the idea that one way to educate people would be to let them see the favorable results in these cases, especially the comparative innocuousness of the artificial anus. I have always told my students that we ought to keep nearby in our great hospitals one of our many successful cases, in which an active person gets along very well indeed with an artificial anus and does not have to curtail his activities in the least. We ought to keep such a patient available to talk to prospective patients.

DR. LINCOLN DAVIS, Boston. Dr. Hayden's paper was extremely well presented and showed first-rate results, and it was impressive to me because it was such an improvement over the statistics of my time. I should like to ask Dr. Hayden or Dr. Lahey, since they both do radical resections in the presence of metastases in the liver, how long the patients live with metastases in the liver.

I have been told that there is a great difference in metastases of carcinoma in the liver between those from the stomach and those from the large intestine, that metastasis to the liver in cases of carcinoma of the stomach is practically a

bar to going on with the resection, whereas that in cases of carcinoma of the large intestine apparently is not. How long can one expect a patient to live with metastases in the liver?

DR. HAYDEN. I am afraid I cannot answer Dr. Davis's question, except by saying that I have knowledge of at least 2 patients who lived for four years with liver metastases. I have always removed the tumor if the liver was not extensively involved, and occasionally even under those circumstances.

It is perfectly obvious that Dr. Lahey's excellent results serve to emphasize what we all know, namely, that large numbers of cases, with increased technical experience, a good organization and first-class anesthesia, entirely aside from the excellent operative ability of the surgeons in the clinic, produce results that one would naturally expect and toward which we all ought to strive.

I am sure that several of my deaths should have been avoided. It is easy to figure this out afterward, but the important thing is to figure it out beforehand.

DR. LAHEY. I can answer Dr. Davis's question because I came prepared to do so. The patients with metastases in the liver who have been operated on, with radical removal of the primary tumor, have lived an average of twenty-five months after operation.

DR. HAYDEN. The patients with recurrences lived an average of two and a half years. Dr. Daland had some figures several years ago on the average duration of life in patients not operated on, which he may want to mention.

DR. ERNEST M. DALAND, Boston. Before this society nine years ago I presented a series of 100 cases of untreated cancer of the rectum, comparing it with a treated series. With absolutely no treatment the average duration of life was fourteen months. We also studied a series of 80 patients who had had colostomy only, and found that their length of life was no greater than that of the untreated group.

I should like to say a word in regard to our experience with cancer of the rectum at Pondville Hospital. At the present time we are operating with a greatly reduced number of beds. In 1941, when we were using 150 beds, we did 23 one-stage abdominoperineal resections, with a mortality of 11 per cent, and 5 colostomies and posterior excisions, with 1 death.

We believe strongly that one of the answers to low mortality is a long preoperative preparation. This can be done better in a state hospital than in some private hospitals. We ordinarily keep a patient for five to seven days and often two to three weeks before operation, getting him in condition so that he can go through an abdominoperineal resection.

I agree thoroughly with Dr. Lahey that the care of the colostomy is extremely important. We do not allow our patients to use bags when they leave the hospital, but quite a number have come back to the follow-up clinics with bags. We think that the patient with a colostomy needs no bag and should have no trouble.

In one of our follow-up clinics last spring I saw 13 patients who had had a radical resection for cancer of the rectum. I had some students with me, so I took pains to inquire about the habits of those patients in regard to their colostomies. Twelve of them said that they had absolutely no trouble. The thirteenth said that he had no control of it, possibly because he was an old man and drank too much beer.

THE FIRST YEAR OF THE EMERGENCY MATERNITY AND INFANT-CARE PROGRAM
IN MASSACHUSETTS

FLORENCE L. MCKAY, M D,* SALLIE SAUNDERS, M D,† AND ETTA BLOOM, A B ‡

BOSTON

THE Emergency Maternity and Infant-Care Program in Massachusetts completed its first year on September 2, 1944. The following discussion relates primarily to the administrative phase of the program rather than to the medical findings. Participating in this program were more than 2000 physicians and 130 hospitals, the latter representing nearly all the 137 licensed hospitals giving maternity service in Massachusetts. During the first year, 13,703 cases were authorized for care. Of these, 12,035 (88 per cent) were maternity cases and 1668 (12 per cent) were infant cases. The total expenditure of funds for the first year was \$591,644 76 ¢.

MATERNITY CASES

During the year in Massachusetts, there were approximately 85,000 deliveries, 14 per cent of which came under this program. Of these cases,

TABLE 1 Cost of Completed Maternity Cases

MONTH OF COMPLETION	NO OF CASES	EXPENDITURE	
		TOTAL	AVERAGE PER CASE
1943			
September to December 1944	71	\$5 683 41	\$80 05
January	105	8,542 12	81 35
February	207	18 441 60	89 09
March	410	38 126 93	92 99
April	507	47 936 28	94 55
May	582	55 475 12	95 32
June	744	71 252 49	95 77
July	1004	98 706 42	98 31
August	791	80 379 11	101 62
Totals	4421	\$424 543 48	
Average			\$96 03

4421 were completed during the year, with a payment of \$424,543 48 (Table 1). In 4276 cases, complete payments were made, in 145 cases, partial

The distribution of these cases in the different classifications of the armed forces were as follows: Army, 71 per cent, Navy, 22 per cent, Marine Corps, 3 per cent, and Coast Guard, 4 per cent. The average amount paid for each case was \$96 03. There was a steady increase in the cost per case throughout the year, from \$80 05 in 1943 to \$101 62 in August, 1944. The stay in the hospital averaged 10 6 days. The lowest amount paid on any one case was \$3 for one prenatal visit. The highest cost for a complicated case was \$380 85.

Of the total amount expended, 58 per cent went to hospitals, 40 per cent to physicians and 2 per cent to miscellaneous charges, such as clinic fees, nursing, ambulance, unusually expensive drugs, transfusions and anesthesia. The payments to private physicians were influenced by the fact that many cases were delivered without medical cost in Army or Navy hospitals or in the wards of the large city hospitals.

Table 2 shows the average amount spent on different types of care given to maternity cases.

TABLE 2 Average Expenditures for Various Types of Service

TYPE OF SERVICE	CASES RECEIVING SPECIFIED CARE		AVERAGE EXPENDITURE PER CASE
	NO	PERCENTAGE OF TOTAL	
Hospital	4259	96	\$58 23
Attending private physician	3608	82	45 58
Consultation	128	3	39 04
Nursing	68	2	7 61
Clinic	348	8	10 82

The average payment to the physician was less than the \$50 fee allowed for complete maternity care because of the fact that some patients moved from Massachusetts, so that they were under a physician's care in this state only a short time.

TABLE 3 Trimester of Pregnancy at Time of Application

TRIMESTER	MONTH OF COMPLETION				ALL CASES	
	NO	SEPT DEC Percentage	NO	JAN -APR Percentage	NO	Percentage
First	1	1	20	2	352	8
Second	1	1	250	20	1472	59
Third	69	98	959	78	2346	53
Totals	71		1229		4421	

payment was made because the patients moved, died or withdrew their applications.

*Director, Division of Child Hygiene, Massachusetts Department of Public Health.
†Assistant director, Division of Child Hygiene, Massachusetts Department of Public Health.
‡Principal statistical clerk, Division of Child Hygiene, Massachusetts Department of Public Health.
§The total expenditure through January 1945 was \$1 195 436 36.

Also, at the beginning many patients were admitted late in their pregnancy, and therefore did not receive complete maternity care under this program. This is more clearly brought out in Table 3, which shows the trimester of pregnancy at the time of application. Because this was the beginning of the program, the first completed cases were naturally in the

third trimester. The second year should give a better picture of the distribution of patients in the three trimesters applying for care.

The distribution of cost according to four-month periods for hospital and medical care (Table 4)

TABLE 4 *Average Payments to Hospital and Attending Private Physicians*

PERIOD	CASES RECEIVING HOSPITAL CARE			CASES HAVING AN ATTENDING PRIVATE PHYSICIAN		
	NO	PERCENTAGE	AVERAGE PAYMENT	NO	PERCENTAGE	AVERAGE PAYMENT
September-December	71	100	\$58.02	33	46	\$40.55
January-April	1194	97	56.89	968	79	43.77
May-August	2994	96	58.77	2607	84	46.32
Totals	4259			3608		
Averages		96	\$58.23		82	\$45.58

shows a fairly steady hospital payment throughout the year. The interesting feature is the increase in the percentage of cases having a private physician from 46 per cent in the first four-month period to 84 per cent, or nearly twice as much, in the last four-month period. The 46 per cent figure may be explained by the fact that the first cases completed were those that were cared for in hospitals where there was no charge for medical care. There was, however, a distinct increase in the number of patients having private medical care. This increase may have been influenced by the fact that after November 15, 1943, the hospital payments were made on the basis of ward cost per patient-day up to \$6. This made it possible, in some cases, for patients to be cared for in semiprivate rooms at ward cost, thus enabling physicians on the courtesy staff to deliver patients in the hospital. The table also shows that the payments to physicians increased gradually during the year, indicating that the later patients came under the program earlier in pregnancy and thus that more prenatal visits were paid for.

Of the 4421 maternity cases, 4357 (99 per cent) were carried through delivery, 25 women had precipitate deliveries in the home. In 4259 cases the program paid for hospitalization, the remainder used some form of hospital insurance.

The outcome of delivery is shown in Table 5.

TABLE 5 *Outcome of Delivery*

OUTCOME	NO	PERCENTAGE
Full term live birth	4026	92
Premature live birth	146	3
Stillbirth	97	2
Abortion	71	2
No report	50	1
Total	4390*	

*Greater than the number of deliveries because there were 33 cases of twins.

There were 4172 live births. Of these, 4026 (96.5 per cent) were full-term and 146 (3.5 per cent) were premature live births. The latter percentage is about that recorded in state well-child conferences and in the hospital reports of premature live

births. The 97 stillbirths represent a rate of 23.3 per 1000 live births, which agrees closely with the rate for Massachusetts in 1943 (23.5). There were 33 cases of twins, or 66 infants, of which 42 were full-term live births, 21 were premature live births

and 3 were stillbirths. Of the 4172 infants born alive, 52 were reported by the obstetric attendant as having died, 51 of them under one month of age. In all probability this does not represent the actual number of deaths. Many obstetricians turn over infants to pediatricians during the first two weeks, especially if they are ill. Thus, there may have been deaths among this group that were not reported by the obstetric attendant.

There were 7 maternal deaths during or after delivery. This represents a rate of 17 per 1000 live births, which compares favorably with the rate for Massachusetts for 1943 (2.0).

INFANT CASES

During the first year of the program, 315 infant cases were completed. An infant case was considered as completed when the infant had reached his first birthday.

The distribution among the divisions of the armed forces closely resembled that of the maternity cases—Army, 74 per cent, Navy, 22 per cent, Marine Corps, 2 per cent, and Coast Guard, 2 per cent.

During the first year infant care comprised payments for the sick infant, for health supervision at well-child conferences and, during August, 1944, only, for immunization (Table 6). In 83 per cent

TABLE 6 *Average Expenditures on Authorized Services for Completed Infant Cases*

TYPE OF CASE	CASES RECEIVING SPECIFIED CARE		EXPENDITURE	
	NO	PERCENTAGE	TOTAL	AVERAGE PER CASE
Total cases	315		\$13,791.73	\$43.78
Care of sick infant	263	83	13,692.23*	52.06
Hospital	111	35	9,806.48	88.35
Attending physician	207	66	3,114.00	15.04
Consultation	18	6	360.00	20.00
Nursing	9	3	93.63	10.40
Immunization	4	1	30.00	7.50
Health supervision at well-child conferences	49	16	69.50	1.42

*Includes \$318.12 spent for services other than the four designated ones.

of the cases payments were for the sick infant. The average cost for infant care was \$43.78, the lowest being 50 cents for health supervision, and the highest \$1480.63 for laryngeal stenosis.

Hospitalization in this group represented by far the greatest cost, even though only 35 per cent of all the infants were hospitalized. These infants had 2005 days of hospital care, an average of 18 1/2 days per case. Nineteen infants died, 8 being under one month of age. Immunization showed a small amount because this service became available only during the last month of the first year.

These 315 cases are too few to form the basis of an analysis from which comprehensive conclusions

may be drawn. They serve rather to indicate the trends to be expected in the increasing numbers that may be reported in the future.

SUMMARY

Certain administrative phases relating to the Emergency Maternity and Infant-Care Program in Massachusetts are discussed, with the aid of statistics derived from the first year of operation.

ACUTE ULCERATIVE COLITIS

-Report of a Case

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ONE of the still unsolved problems in medicine is a condition described in the medical literature as "chronic ulcerative colitis." As yet no completely successful treatment has been evolved, and many confusing reports on the efficacy of various therapeutic measures are still to be found. Most authors agree concerning the symptomatology and consider that the disease is essentially chronic in nature, with acute exacerbations as a characteristic feature. The majority of writers also agree that a chronic ulcerative colitis may be caused by several different agents. In one form of the disease, for which no specific cause has as yet been found, the term "nonspecific ulcerative colitis" is employed.

The therapy of this form of ulcerative colitis is still a matter of personal experience and opinion. Reports of the results of dietary management, chemotherapy, serum therapy and different methods of surgical interference are reported with enthusiasm by some, but are discredited by others who have experienced no success with these methods.

A feature that is predominant in all the cases of nonspecific ulcerative colitis is the nervous personality of the patient, or some manifestation of an abnormal psychologic condition.

A survey of the literature on ulcerative colitis indicates that the term "chronic ulcerative colitis" is not satisfactory. There are some cases in which the disease runs an acute fulminating course that might properly be called "acute ulcerative colitis." This manifestation, which has been reported only occasionally, is of importance because of the tendency toward a rapid fatal outcome. Only in a few cases do therapeutic measures seem to be successful, and even in these a critical observer asks himself whether the recovery occurred independently of them or because of them.

The importance of an early diagnosis in acute fulminating cases is obvious, but this may be difficult at times, especially if the features of the disease are confusing and if sigmoidoscopy cannot be done. The following case history serves as an illustration.

CASE REPORT

E. F., a 29-year-old, married woman, was admitted to the Harrington Memorial Hospital on August 8, 1944. Four days previous to admission, she began to have diarrhea. She had eleven bowel movements on the 1st day, and the stool contained some blood and mucus and was very watery. There was no pain. The appetite was good, but the patient slept poorly. The day previous to admission she could take no food without vomiting.

The past history revealed little information. The patient had never been seriously ill. She had borne a child 8 years previously. Her married life was happy. Menstruation was regular. She had always been nervous, and the only time when she was mentally contented was when she worked in a factory and did not have time to think about herself. Six years previously she spent much of her time with a friend who had colitis and who talked incessantly about her disease. The patient became afraid that she would contract it, and possibly as a result had an attack of diarrhea. A diagnosis of colitis was made, but was never confirmed by an examination. During the last 5 years, she had several attacks of diarrhea, but did not move her bowels more than three or four times a day, and the attacks never lasted more than 3 days. These attacks were always connected with excitement or worry.

During the 7 months before admission the patient took care of her mother, who was suffering from cancer of the intestines and bladder. She thought that she might get cancer, and worried continually. She was also upset by her father, who was a chronic drinker and came home every night intoxicated. Once he tried to commit suicide by jumping out of the window, and she had to hold him back. From then on she stayed up every night until he was safely in bed. Her husband's joining the Navy added to her worries. Two weeks after the death of her mother, she left her home and went to visit her aunt. Ten days later her acute illness began.

Physical examination showed a thin, sick-looking woman, who was extremely nervous. The weight was 98 pounds (40 pounds underweight). The blood pressure was 110/80, the pulse 128 and the temperature 98.6°F. The tongue was coated. The lungs were normal. The heart was within normal borders, with the action regular but accelerated. There were no murmurs or abnormal accentuations. The abdomen was sensitive and somewhat tender throughout. The spleen and liver were not enlarged, and no tumor masses were palpable.

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Rectal examination revealed no abnormality. There was a slight exophthalmos, and a tremor of the hands and tongue. The reflexes were exaggerated. There was a slight papular skin rash.

The urine showed no albumin, sugar or bile, microscopical examination was negative. The hemoglobin was 87 per cent

watery. Since all the examinations, including x ray study showed no sign of colitis, it was thought that the patient had an intestinal infection, and she was treated accordingly. A sigmoidoscopy was proposed, but before the necessary arrangements could be made the patient insisted on going home, leaving the hospital against medical advice on the 5th day.



FIGURE 1

and the color index 1.05. The red-cell count was 4,160,000 and the white-cell count 19,500, with 77 per cent neutrophils, 19 per cent lymphocytes and 4 per cent mononuclears. Bacteriologic examinations of the stool and urine for paratyphoid and dysentery bacilli were negative. X-ray examination of the colon on the 3rd day showed no gross pathologic change (Fig. 1).

On the 2nd day, the temperature gradually began to rise (Fig. 2). The stools showed no blood or mucus but were very

Before she left, treatment with sulfaguanidine was started, and this was continued in her home by her physician.

The patient was readmitted on August 28. While at home, she had discontinued the sulfaguanidine treatment for some time and had then recommenced it in smaller doses. She had been running a temperature of 99°F in the morning and one of 101 to 102°F at night. She had had several watery bowel movements daily and had lost 7 pounds. Two days before admission she discovered a skin rash on both knees.

The physical findings were not much changed from those on the first admission, except that the patient appeared to be much sicker. The abdomen was slightly distended, and there were gurgling sounds in the intestines. There was slight pain on pressure on the right side of the abdomen. There was a skin rash on both knees, with round, oval pale-red swellings, slightly elevated and painful to touch. The pulse was 150 to 160 and of poor quality. The blood pressure was 110/90. The white-cell count remained at 15,000. Rectal examination again proved negative. The patient was apprehensive and anxious. She still had four to eight watery bowel movements every 24 hours, which never contained blood or mucus. She ran septic temperatures that reached 103°F at night and 99.4°F in the morning.

Three days after the second admission, the right knee joint became swollen and painful. The next day a slight systolic murmur was heard over the apex and mitral area. The spleen appeared to be enlarged and painful. The white-cell count remained between 15,000 and 20,000. The urine and stool were negative. An agglutination test for undulant fever and a blood culture were negative.

The clinical picture at this stage of the disease included a septic temperature (Fig 2), a rapid pulse of poor quality, a

sarv. This was performed on the following day. The cecum was thickened and red. Because of the patient's weakened condition, the surgeon did not explore farther. After the operation, intensive parenteral fluid therapy was administered, including plasma, blood and dextrose, but in spite of this her condition became worse daily. The temperature rose again, as did the white-cell count.

On the 10th day following operation, the patient developed a psychosis. She became extremely aggressive but was easily quieted. On the 11th day she became noisy, screamed if anyone came near her bed and insisted that the nurses and physician were going to poison her. On the same day the temperature rose to 103.4°F and the white-cell count to 30,000, and the patient died.

Autopsy (performed by Dr William Freeman). The entire colon had many ulcers, five of which had perforated the bowel at its rectal end. The serosa of these perforated areas was dark-red, soft and mushy and was surrounded by a thick bank of greenish-gray fibrinous exudate. There was practically no free fluid pus. In the remainder of the colon, beginning at the cecum, there were relatively few ulcers, which were shallow and involved only the mucosa. The edges of these ulcers were serrated but not hemorrhagic. Distally the

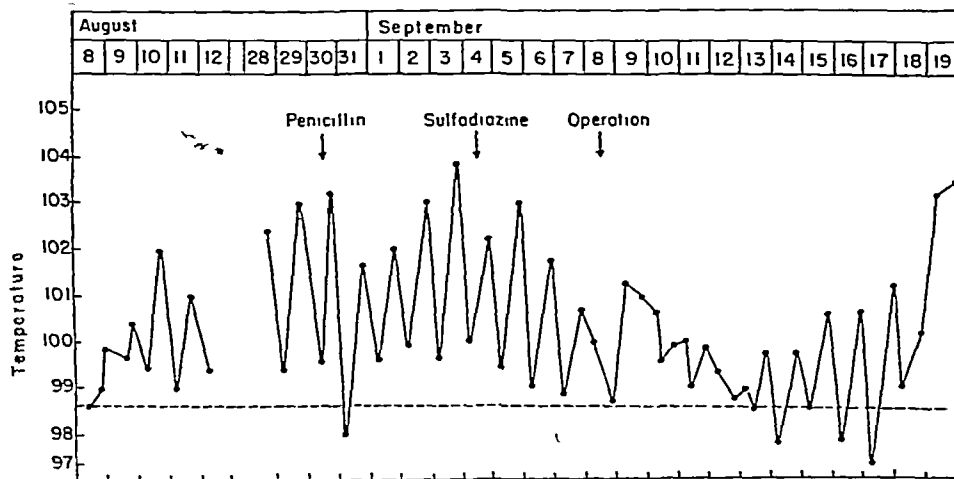


FIGURE 2

systolic murmur, an enlarged spleen, skin eruptions, an acute inflammatory swelling of one knee joint and a high white-cell count — the perfect clinical picture of a septicemia. There was still no objective proof of colitis. The negative blood culture proved nothing against the diagnosis of septicemia because of the previous medication with sulfaguanidine. An electrocardiogram merely showed a sinus tachycardia. An x-ray examination of the chest was negative.

On the 10th hospital day, 3 weeks after the first barium enema, another x-ray film was taken. This showed a tremendous change in the colon. Its outline presented a typical saw-tooth appearance along its entire course, characteristic of advanced ulcerative colitis (Fig 3). The last third of the large intestine seemed to be deprived of most of its mucosa. These x-ray findings established the diagnosis.

Up to this date every therapeutic measure had proved ineffective. When the diagnosis of probable septicemia was established, penicillin was given in doses up to 100,000 units every 24 hours for 5 days. Neither the patient's condition nor the temperature improved in any way, and on the 6th day this treatment was discontinued and sulfadiazine treatment was begun. This seemed to be more effective, inasmuch as the temperature slowly decreased and the white-cell count fell from 14,000 to 10,000. The enlargement and tenderness of the spleen, the swelling of the right knee joint and the skin rash disappeared.

After the x-ray examination had established the seriousness of the colitis, it was decided that an ileostomy was neces-

sary. This was performed on the following day. The cecum was thickened and red. Because of the patient's weakened condition, the surgeon did not explore farther. After the operation, intensive parenteral fluid therapy was administered, including plasma, blood and dextrose, but in spite of this her condition became worse daily. The temperature rose again, as did the white-cell count.

SUMMARY

A case of acute ulcerative colitis is presented, with several unusual clinical features indicative of the infectious process. These included a large tender spleen, swelling of the knee joint and erythema nodosum. Death occurred from the severity of the infectious process and multiple perforations of the bowel.

The lack of response to adequate penicillin therapy was striking, and suggests that this drug is of little

value in acute nonspecific ulcerative colitis. Similarly, an ileostomy was ineffective, presumably because of the fulminating nature of the condition.

Failure to make an early diagnosis was undoubtedly due to the fact that sigmoidoscopy could not be performed. The importance of this maneuver as a di-



FIGURE 3

The apparent response to sulfadiazine indicates that this form of chemotherapy should be fully attempted over an adequate period of time in cases of this severity.

agnostic measure in unexplained diarrhea is stressed. The importance of psychologic factors in aggravating the condition is demonstrated.
284 Main Street

MEDICAL PROGRESS

BODY-FLUID PHYSIOLOGY THE RELATION OF TISSUE COMPOSITION TO PROBLEMS OF WATER AND ELECTROLYTE BALANCE*

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THE following paper summarizes recent work on the chemical structure of the body in as much as it is related to some of the problems of water and electrolyte balance. Some of the concepts are based on work that has not yet been confirmed, but enough is established to give a tentative outline of the changes in composition of intracellular as well as extracellular fluids.

CHEMICAL ANATOMY

From the point of view of balance of water and electrolyte, the chemical anatomy can be described in terms of three tissues. These are chosen because

water and electrolyte will not enter into the subsequent discussion.

The second category of tissues makes up the extracellular fluids and is typified by blood plasma. Table 1 gives representative examples of extracellular fluids. They all contain large amounts of sodium and chloride and relatively little potassium and magnesium. Although interstitial fluid contains much less protein than does blood plasma or lymph, it is not protein-free.³ The composition of the various gastrointestinal fluids and sweat is dependent on the activity of the glands. Cerebrospinal fluid contains more chloride than an ultra-

TABLE 1 *Approximate Composition of Various Extracellular Fluids*

FLUID	HCO ₃ mM/l	Cl mM/l	Na mM/l	K mM/l	Ca mM/l	Mg mM/l	PROTEIN gm/l	WATER gm/l
Serum	25	100	142	4.3	2.5	1.7	70	940
Ultrafiltrate of serum	28	111	145	3.3	1.6	1.2		993
Spinal fluid	21	125	147	2.8	1.7			993
Gastric juice	0	145	20	8				993
Bile	38	103	140	8				990
Pancreatic juice	110	40	140	5				993
Jejunal juice	30	110	138	5				993
Sweat	0	85	82	5	2.5			993

of their size, and because their peculiar chemical composition characterizes other tissues, both as to composition and to the types of change that take place.

The first tissue is bone, which contains almost all the body calcium and extracellular phosphorus. The molecular ratio of calcium to phosphorus in bone is 1.057. This fact enables one to calculate the balance of cellular phosphorus from the balance of calcium and phosphorus. It is not usually recognized that calcified material contains about 1 mole of sodium for every 30 moles of calcium.¹ Thus, bone sodium is equivalent to about 10 per cent of the total body sodium in babies and about 33 per cent of that in adults.² Since this sodium is not available to the rest of the body fluids when combined in the calcified matrix, bone sodium can affect other body fluids only when extreme changes in calcification are taking place. Since significant fluctuation in the amount of bone calcium is not likely to occur in the short periods of time when a physician is concerned with problems of water and electrolyte balance, the effect of bones on tissue

filtrate of plasma, owing to some peculiarity of the so-called "blood brain barrier." All the extracellular fluids are derived from blood plasma, and a protein-free ultrafiltrate plasma may be used to represent the composition of extracellular fluids as a whole. Altogether, extracellular fluids make up 25 to 30 per cent of the body weight in babies and 20 per cent of that in adults. Total extracellular electrolyte is approximately equal to the volume of extracellular fluids times the concentration of the various electrolytes in an ultrafiltrate of blood plasma.

It is obvious that the preservation of the integrity of the extracellular fluids is intimately connected with the balance of sodium and chloride. The chief organ that regulates these fluids is the kidney. Indeed, the urine may be considered a highly modified filtrate of plasma that is elaborated and excreted for this purpose. It is obvious that extracellular fluids may increase or decrease in volume, as in edema and dehydration, they may show increase or decrease in electrolyte concentration, and there may be an increase or decrease in bicarbonate concentration, as in alkalosis or acidosis. Some mention of the effects of these various disturbances on total body electrolyte is given below.

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The third category of body fluids comprises the intracellular fluids. In addition to organic material and water, the cytoplasm is made up of relatively large amounts of potassium, magnesium and phosphorus and small amounts of sodium and chloride. Table 2 shows analyses of different tissues together with the probable proportions of extracellular and intracellular water and the probable concentrations of certain constituents per kilogram of intracellular water. The compositions of intracellular fluids are

this fashion, but heart muscle shows no demonstrable change in intracellular water in response to changes in concentration of extracellular sodium, and brain tissue tends to lose potassium⁶ and to keep intracellular water relatively constant. Intracellular sodium replaces deficits of skeletal and cardiac muscle potassium, but true deficits of liver potassium have not been demonstrated except in certain stages of shock.⁷ The errors involved, however, in considering that all intracellular fluids react like

TABLE 2 Composition of Various Tissues* and Probable Composition of Intracellular Fluid †

Tissue or Fluid	CL	NA	K	P	PROTEIN	WATER		TOTAL
	mM	mM	mM	mM	gm	EXTRA-CELLULAR gm	INTRA-CELLULAR gm	gm
Skeletal muscle	6	8	48	33	96	37	308	345
Cardiac muscle	19	24	40	34	88	129	281	410
Liver	11	11	30	36	75	65	205	270
Brain	25	37	67	67	69	170	363	533
Intracellular fluid								
Skeletal muscle	3	7	155	107	306			
Cardiac muscle	7	15	142	121	310			
Liver	12	5	145	176	366			
Brain	3	27	184	184	190			

*Expressed as amounts per 100 gm of fat free solids

†Expressed as amounts per 1000 gm of intracellular water

similar but not identical. The characteristic feature is a high concentration of phosphorus, potassium and magnesium and a low concentration of sodium and chloride. The amount of intracellular water is chiefly dependent on the balance of potassium but is indirectly influenced by the concentration of extracellular sodium.^{4,5}

From the point of view of the body as a whole, total intracellular fluids may be represented by the intracellular phase of skeletal muscle. This is permissible because 40 per cent of the body weight is made up of muscle, and this accounts for about

that of skeletal muscle are not large enough to invalidate this assumption as a means of visualizing a first approximation of changes in the composition of body water and electrolyte as a whole.

SCHEMATIC REPRESENTATION OF BODY WATER AND ELECTROLYTE

To represent the makeup of the body, Table 3 shows the approximate composition of a 10-kg infant.* Extracellular fluid is represented as 2.5 kg of fluid having the composition of an ultrafiltrate of plasma. Intracellular fluids are represented by

TABLE 3 The Extracellular and Intracellular Fluids in a Normal 10-Kg Child

FLUID	HCO ₃		CL		NA		K		SOLIDS		WATER
	mM/kg	mM	mM/kg	mM	mM/kg	mM	mM/kg	mM	gm/kg	gm	kg
Extracellular											
Concentration	28		111		145		3		8		2.5
Amount		70		277		362					
Intracellular											
Concentration*	10		3		12		157		306		4.5
Amount		45		15		54†		706†		1377	

*The composition of intracellular fluid is based on analyses of cat muscle.

†The table shows the usual concentrations and amounts of intracellular sodium and potassium. Actually, intracellular sodium may be practically zero and the concentration of intracellular potassium about 10 per cent lower in essentially normal rats and cats. Thus, the total intracellular sodium may vary from a trace to 54 mM and the potassium from 640 to 706 mM.

70 per cent of the total intracellular fluid. For a schematic presentation, the high proportion of muscle water is fortunate, since the changes in composition of muscle under various conditions can be described with considerable confidence.^{4,5} Thus, osmotic equilibrium between the intracellular and the extracellular phases of muscle is brought about by shifts of water into or out of the cells so as to bring about a change in electrolyte concentration about half as great as that in extracellular fluids.⁵ No shift of cations across the membranes seems to be involved. Liver tissue also reacts in

4.5 kg of fluid having the composition of the intracellular phase of the muscle. The data are based on analyses of cat muscle, but human muscle resembles cat muscle quite closely. Since it has been found⁸ that the composition of the muscle of rats shows certain variations without abnormalities in the serum, the limits of these variations are shown in a footnote to the table. It should be stated, however, that both rats and cats tend to have the higher

*An adult would be represented by the same proportions except that extracellular water would be less—20 per cent of body weight instead of 25 per cent. The tables represent only approximations, but since the important relations are quantitative, tables rather than diagrams are the best method of presentation.

levels of intracellular potassium and sodium, and this fact justifies the assumption that these values are frequent. When serum potassium is abnormally high, muscle potassium may reach even higher levels, usually with apparent loss of intracellular sodium.⁸ As is pointed out below, there is a tendency toward reciprocal relation between intracellular sodium and potassium in muscle. The low normal levels of muscle potassium, however, are not always accompanied by gains in intracellular sodium, and the high normal levels of muscle potassium do not necessarily lead to low intracellular sodium. Attention is directed to the considerable normal variation in body sodium and potassium that may arise from variations in so-called "normal" cellular composition of intracellular fluids.

The evidence for intracellular chloride is indirect⁵ and theoretical.⁹ Some evidence indicates that its concentration equals that of potassium in extracellular fluids. It constitutes a sufficiently small and constant fraction of total extracellular chloride so that it need not be considered in the present discussion.

Table 3, then, shows what may be considered the normal partitions in tissue composition when the normal variations of extracellular concentrations and volumes are not taken into consideration. Subsequent paragraphs will bring out the effects of normal as well as abnormal variations in the composition of intracellular fluids.

CHANGES IN BODY FLUID INVOLVING EXTRACELLULAR ELECTROLYTE

Previous discussions of the problems of body water and electrolyte have assumed that the cell membranes are practically impermeable to cations.¹⁰⁻¹² This surmise is known not to be true, for it has been demonstrated that both sodium and potassium readily cross cell membranes. Nevertheless, the distribution of these cations remains such that many phenomena can be described by assuming that adjustments to changes in the sodium concentration in extracellular fluids will be largely brought about by shifts in water. Thus, with a decrease in concentration of serum sodium, water enters the cells so as to reduce the concentration of intracellular potassium in muscle and liver and probably many other tissues.⁵ If there is increase in concentration of serum sodium, water leaves the cells so as to increase the concentration of intracellular potassium. The process is the same as the swelling and shrinking, respectively, of erythrocytes in hypotonic and hypertonic salt solutions. Hence, the volume of extracellular fluids depends chiefly on the total amount of extracellular sodium and extracellular water can be maintained at the expense of a drop in serum sodium concentration. Diminution of extracellular volume frequently accompanies abnormal concentrations of extracellular electrolyte and probably accounts for the fact that such con-

ditions are grouped together under the term "dehydration." Total body water, however, may be normal when serum concentrations are low because the cells contain too much water. Also, total electrolyte is usually diminished in amount when serum concentrations are high, because high concentrations usually mean that there is not enough water available for the kidney to carry out its function of adjusting electrolyte concentration. Generally, some sodium and chloride have been excreted before the shortage of water has led to the rise in concentration. The important point is to realize that the central feature of clinical dehydration is practically always a deficit of extracellular electrolyte, and that this may or may not involve gross deficit in total body water.

The mechanisms of the various symptoms of dehydration are not clear. Space is not available for discussion of these features, but the practical point that loss of body water and electrolyte leads to shock needs emphasis. Loss of extracellular electrolyte usually involves decrease in plasma volume and a tendency to lose plasma proteins. It is for this reason that patients suffering from dehydration must be given transfusions as well as salt solution. For the same reason a patient in dehydration must never be subjected to procedures leading to shock until his deficit of sodium chloride has been replaced, and frequently transfusions of blood are also indicated. This point is illustrated by the fact that the recent drop in operative mortality in such a surgical emergency as intussusception correlates with the preoperative care rather than with the time of operation. Decrease in glomerular filtration accounts for the poor renal function of dehydrated patients, and salt as well as water is required to restore urine volumes.

Experimental and clinical observations indicate that dehydration is usually accompanied by a relatively greater loss of sodium and chloride than of water and that this results in a decrease in the concentrations of extracellular electrolyte. In animals the maximal loss of extracellular electrolyte that is compatible with life is one third to one half of the total extracellular electrolyte. This is equivalent to 80 to 100 cc per kilogram of body weight of physiologic saline solution or some fluid more closely resembling interstitial fluid.

Table 4 shows the probable state of body water and electrolyte that results from the loss of about one third of the extracellular electrolyte without change in total body water. The figures are based on data obtained from analyses of cat muscle and represent fairly closely what occurs in many patients. Tables 3 and 4 should be compared to appreciate the deviations from normal. Note that the shift of water into the cells does not diminish the intracellular concentration of potassium as much as does the decrease in extracellular concentration of sodium.⁵ This representation conforms to direct

analyses of tissues⁶ and has been indirectly confirmed by other types of observation.¹³ The finding indicates that some intracellular compounds, presumably those combined with potassium, do not dissociate to the same degree under all conditions. In the schematic representation it was assumed that 10 mM (millimoles) of sodium was transferred from intracellular to extracellular fluids. Tissue analyses suggested but did not prove this type of reaction in cats subjected to depletion of extracellular electrolyte.⁵ The scheme indicates that about 600 cc of physiologic saline solution should correct all the defects in tissue composition if the kidneys function adequately.

Certain observations¹⁰ suggest that following loss of extracellular electrolyte the kidneys tend to restore the concentrations to normal by excreting water. In the above schema this could be done by the excretion of 0.6 kg of water. Theoretically this would leave intracellular fluids normal but reduce extracellular water to 1.9 instead of 2.07 kg. With small losses of extracellular electrolyte

in the present discussion to represent a disturbance in tissue composition. When the various items are left in the body in abnormal proportions, a disturbance in body water and electrolyte has developed.

As shown in Table 3, a considerable normal variation in intracellular electrolyte is indicated. Thus, if all intracellular sodium leaves the cells, an amount of sodium (54 mM) is made available to extracellular fluids that is equivalent to about one sixth of the total extracellular sodium. In terms of acid-base equilibrium this amount of sodium could increase the sodium available to form bicarbonate by an amount equivalent to three fourths of the normal sodium bicarbonate of extracellular fluids. On the other hand, if the muscle started with low intracellular sodium, increase in intracellular sodium to the usual higher figure would have a corresponding effect in decreasing extracellular sodium, especially that combined with bicarbonate. Both types of reaction probably take place especially in degrees not involving all the intracellular sodium. These small shifts of intracellular sodium, however, are

TABLE 4 The Extracellular and Intracellular Fluids in a Dehydrated 10-Kg Child *

FLUID	HCO		CL		NA		K		SOLIDS		WATER
	mM/kg	mM	mM/kg	mM	mM/kg	mM	mM/kg	mM	gm/kg	gm	kg
Extracellular Concentration	24		101		131		33				
Amount		50		210		275		7			2.07
Intracellular Concentration	10		33		9		143		280	1377	4.93
Amount		49		16		44		706			

*It is assumed that no water has been lost and that the loss of electrolyte is 87 mM of sodium and 66 mM of chloride; the composition of the intracellular fluid is based on analyses of cat muscle.

this type of reaction occurs, but with large deficits of sodium and chloride the kidneys excrete water slowly and tend to preserve volumes at the expense of concentrations.¹⁴⁻¹⁶

Dehydration may be caused by abnormal diuresis, —adrenal insufficiency, diabetes, hyposthenuric nephritis and so forth, —diarrhea, sweating or vomiting. Furthermore, localization of extracellular electrolyte at the site of trauma or a burn affects the rest of the body in much the same manner as does loss from the body. Each type of loss tends to have certain characteristic features. These have previously been adequately described.¹⁰⁻¹² For this reason the rest of the discussion will be concerned with intracellular changes.

CHANGES IN BODY FLUIDS INVOLVING INTRACELLULAR ELECTROLYTE

During starvation, fever and certain other disturbances, cellular structures may be consumed as a whole. In this case, nitrogen, potassium and phosphorus are excreted together with water in the proportions that make up the tissues consumed. This type of change leads to loss of body water and electrolyte, but the remaining tissues are relatively normal, and such losses are not considered

difficult to prove in patients, and considerable study will be necessary to determine the frequency and extent of such changes under various circumstances.

Studies have shown that practically all intracellular sodium is transferred to extracellular fluids in one type of acidosis. This observation was made in infants subjected to a procedure leading to retention of chloride without change in total body sodium.¹⁷ Further study will be necessary to determine how frequently a similar transfer occurs in other types of acidosis and whether other types of change in extracellular fluids can produce the same shift of sodium out of the cells. As long as the shifts of sodium in the cells are within the normal range, such deficits as develop involve only sodium and chloride and hence can be treated with sodium chloride and sodium bicarbonate.

Under a number of conditions potassium can be lost from the body in excess of the loss of nitrogen or phosphorus, thus leaving the cells relatively poor in potassium. This type of change in intracellular composition has been best demonstrated in skeletal muscle and occurs in the heart and brain, but has not yet been demonstrated in other tissues. Table 3 shows a fairly large normal variation of potassium,

but beyond this range the change is abnormal and sodium tends to replace potassium in almost equivalent amounts. As much as one half the muscle potassium may be replaced by sodium in experimental animals, and evidence is accumulating that similar if less marked changes can occur in human beings.

Table 5 represents the probable water and electrolyte of the body that result when about one third of the intracellular potassium is replaced by sodium and no gross change in extracellular fluids accompanies the change in intracellular electrolyte. Under these circumstances, intracellular sodium is equivalent to about two thirds of the total extracellular sodium. The concentration of serum potassium is represented as low since low serum potassium occurs frequently, but by no means always, when muscle potassium is deficient. Serum chloride is represented as low, and bicarbonate high, although this type of change is also not always present. The picture is probably exaggerated over the ones that are encountered clinically, but subsequent discussion

tions of sodium chloride and glucose while receiving no food by mouth.²⁴ On the other hand, potassium deficit may be produced through losses in the stools. Low serum potassium has been found in 2 cases of sprue, administration of potassium by mouth produced clinical improvement.²⁵ Such large stool losses of potassium in relation to nitrogen as were demonstrated many years ago²⁶ show that deficit of potassium must be an important feature of many cases of infantile diarrhea. I have studied a case of severe diarrhea in an infant that showed such retentions of sodium, chloride, potassium and nitrogen during recovery from marked dehydration and acidosis that the data can only be interpreted as indicating that a deficit of potassium was present before treatment. The data show that abnormal amounts of sodium had entered the cells to replace the deficit of potassium. The patient apparently developed acidosis because sodium went from the extracellular fluid to the cells and not because sodium was lost from the body. Hence the acidosis was chiefly dependent on the deficit of body potas-

TABLE 5 The Extracellular and Intracellular Fluids in a 10-Kg Child after Depletion of Potassium *

FLUID	HCO		CL		NA		K		SOLIDS		WATER
	mM/kg	mM	mM/kg	mM	mM/kg	mM	mM/kg	mM	g/kg	gm	kg
Extracellular Concentration	34		105		145		2.2				
Amount		85		262		362		5.5			2.50
Intracellular Concentration	10		2.2		55		112		327		
Amount		42		9		230		476	1377		4.20

*It is assumed that some loss of intracellular water had occurred that the weight hence became 9.7 kg. and that the depletion of potassium was about one fourth of the low normal content. The changes in intracellular water were suggested from analyses of rat muscle.

shows that considerable deficit of potassium occurs clinically, and only further study can assay the frequency and degree of the deficit.

Loss of muscle potassium may occur from three causes. First, a negative balance of potassium develops from a discrepancy between the rate of intake and output. Since the stools and urine always contain potassium, a diet low in potassium produces deficit of muscle potassium with replacement by sodium. This was first demonstrated in growing rats,¹⁸ and the same condition was found independently in adult rats.^{8,19} The same abnormal composition of muscle can be produced on normal diets by increasing the rate of renal excretion of potassium. Desoxycorticosterone acetate has this effect to a marked degree.^{8,19,20} Adrenocortical extract, testosterone and estrogens exhibit it to a less degree.^{19,21} Some patients with Cushing's syndrome apparently develop potassium deficit. This is indicated by reports of cases showing high concentration of bicarbonate, high or normal sodium and low chloride and potassium in serum.^{22,23} The alkalosis and low chloride do not respond to sodium chloride but do respond to potassium salts. Renal loss of potassium can apparently also be excessive in patients receiving parenteral therapy with solu-

sium. This interpretation of the balance data assumes an abnormal intracellular fluid in the muscle such as is represented in Table 5. Such a state has been found by analyses of the muscle of an infant dying of diarrhea.⁷ In all the above types of potassium deficit, the changes in intracellular fluids are dependent on loss of body potassium.

A second type of deficit of intracellular potassium is apparently dependent on a changed equilibrium in intracellular fluids in states of marked alkalosis. This surmise was first suggested by observations on 2 patients suffering from a congenital defect in intestinal absorption leading to profound alkalosis as a result of loss of water, chloride and sodium in the stools.^{27,28} During the development of an extremely low serum chloride and an extremely high bicarbonate, more chloride was lost than sodium, and the changes in serum concentration demonstrate that sodium entered the cells and displaced equivalent amounts of potassium. The deficit of potassium developed owing to excretion in the urine in two periods and in the stools in one.²⁹ For this reason it seems likely that the potassium was freed from the cells owing to a disturbed equilibrium in the cells rather than to a necessity of the kidneys to excrete potassium instead of sodium. The suggestion

of a disturbed equilibrium in alkalosis tending to produce high intracellular sodium and low potassium has been confirmed by direct analyses of rat muscle following the production of alkalosis due to loss of chloride without sodium. After several days, this type of alkalosis leads to a change in muscle composition characterized by high intracellular sodium and low potassium.⁷ It is likely that the same reaction to alkalosis explains the muscle composition of rats kept for several days at a low atmospheric pressure.²⁹ Future investigations should show whether the same change in muscle composition occurs in some cases of pyloric obstruction. That such a change is likely is suggested by the relative ineffectiveness of treatment with sodium chloride in certain patients. If the loss of electrolyte were purely extracellular, sodium chloride would provide adequate treatment.

A third possible mode of development of relative deficit of potassium is suggested by observations in a patient receiving testosterone who showed low serum potassium levels and a greater retention of nitrogen relative to potassium than is ordinarily considered to be compatible with the formation of normal muscle.³⁰ The data suggest that deficit of potassium may develop during rapid storage of nitrogen, although the experiments are complicated by previous administration of desoxycorticosterone acetate.

Recognition of the above intracellular changes is bound to modify the concepts of treatment, but much work remains to be done before a practical guide can be given for the treatment of the disturbance of the intracellular fluids. In the space available a few obvious implications will be mentioned.

First, acidosis does not involve changes in extracellular fluids alone. The dose of bicarbonate should take this fact into account. To restore the concentration of serum bicarbonate, the concentration of bicarbonate must first be raised in the total extracellular fluid. The following formula calculates the amount necessary in millimoles of sodium bicarbonate or cubic centimeters of molar sodium lactate.

Extracellular water \times deficit of carbon dioxide = 0.2 body weight \times (25-CO₂) = mM sodium bicarbonate or cc molar sodium lactate,

when the body weight is expressed in kilograms and the carbon dioxide in millimoles per liter. If extracellular water is low, the necessary amount of sodium chloride and sodium bicarbonate together with water must be given to replace this deficit. This requirement is satisfactorily taken care of by physiologic saline solution in the amounts appropriate to the degree of clinical dehydration. If intracellular sodium has been depleted, this additional requirement must be administered before tissue electrolyte can become normal. Intracellular sodium in millimoles is equal to about ten times half the body weight. It is interesting that this analysis of the three sources of the deficit of sodium in acidosis

fits the frequently used formula for calculating the dose of sodium bicarbonate, namely,

Half body weight \times deficit of carbon dioxide = 0.5 body weight \times (25-CO₂) = mM sodium bicarbonate or cc molar sodium lactate,

where the body weight is expressed in kilograms, and the carbon dioxide deficit in millimoles per liter.

The implications of abnormally high intracellular sodium are different, since this implies a deficit of potassium that renders the high intracellular sodium unavailable to extracellular fluids until potassium is restored. Thus, in acidosis the dose of bicarbonate may be the same in a patient with potassium deficiency, as is indicated above, except that as potassium is retained, a tendency to alkalosis may develop. On the other hand, a combination of the chlorides and bicarbonates of both sodium and potassium may turn out to be the most effective treatment of cases of acidosis with potassium deficit.

In the alkalosis of certain cases of Cushing's syndrome, the abnormal serum composition tends to persist until potassium salts are administered.³¹ The refractoriness of some cases of pyloric obstruction to sodium chloride suggests an analogous state of deficit of potassium. Future research may demonstrate that the chlorides of both sodium and potassium are indicated in the treatment of certain cases of alkalosis.

In any case, deficits of both potassium and sodium chloride are factors in disturbed balance of water and electrolyte requiring practical as well as theoretical consideration. Moreover, deficiency of body potassium is known to be an extremely serious condition, since it produces necrosis of the heart muscle³² and under unusual circumstances muscular paralysis, which is relieved by potassium.³³ There can be no doubt that the treatment of Addison's disease with desoxycorticosterone acetate has produced heart lesions and death from cardiac failure, but moderate deficits of potassium may be relatively harmless. Since most foods are rich in potassium, most patients tend to recover from potassium deficiency when they can eat. Others require specific treatment with potassium salts.

Administration of potassium salts must be undertaken with caution until more quantitative facts are available concerning the amount of the deficit, the cases requiring treatment and the effect of the administration of potassium salts. Caution is necessary particularly for parenteral therapy, since a rise of extracellular potassium concentration to about 10 mM per liter causes heart block. Potassium salts can be given by mouth with little hazard if renal function is good. Future study will doubtless show a fairly wide field for potassium therapy.

SUMMARY AND CONCLUSIONS

The disturbances in water and electrolyte balance are discussed with emphasis on the changes in intracellular electrolyte. There is a normal variation

intracellular sodium equivalent to about one sixth of total extracellular sodium. This intracellular sodium is available to extracellular fluids in some cases of acidosis.

If potassium is lost from muscle cells beyond a limited amount, sodium tends to enter the intracellular fluid in about equivalent amounts. This type of exchange can involve almost half the muscle potassium, and under these circumstances intracellular sodium is equal to over half the total extracellular sodium.

This replacement of muscle potassium by sodium occurs as the result of potassium loss owing to diarrhea, abnormal renal excretion as a result of the presence of certain steroids (desoxycorticosterone and those concerned with hyperadrenalism) and following deficient intake.

Potassium probably tends to be displaced by sodium in marked alkalosis and perhaps during rapid storage of nitrogen under the influence of testosterone.

It is pointed out that transfer of extracellular sodium to intracellular fluids tends to produce acidosis or to decrease alkalosis and that the reverse process occurs when intracellular sodium enters extracellular fluids. The implication of these changes regarding therapy are briefly discussed.

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE EXECUTIVE COMMITTEE OF THE COUNCIL

Held in Lieu of the Annual Meeting of the Council, May 23, 1945

THE meeting was called to order by President Bagnall on Wednesday, May 23, 1945, at 10 30 a m, in Sprague Hall, 8 Fenway, Boston

The following members of the Executive Committee were present

President Elmer S Bagnall
President-Elect Reginald Fitz
Secretary Michael A Tighe
Treasurer Eliot Hubbard, Jr

Barnstable William D Kinney
Berkshire Isaac S F Dodd
Bristol North William H Allen
Bristol South Edwin D Gardner
Essex North Frank W Snow
Essex South Walter G Phippen
Franklin William J Pelletier
Hampden William A R Chapin
Middlesex East Edward M Halligan
Middlesex North William F Ryan
Middlesex South Dwight O'Hara
Norfolk Charles J Kickham
Norfolk South Henry A Robinson
Plymouth Peirce H Leavitt
Suffolk Donald Munro
Worcester Ralph S Perkins
Worcester North C Bertram Gay

The following chairmen of committees were present Francis C Hall, Roy J Ward, Howard F Root, Frank R Ober, Charles F Branch, Z William Colson, Richard M Smith, Arthur W Allen, W Richard Ohler, Albert A Hornor, William E Browne, Daniel B Reardon, Charles E Mongan, Nathaniel W Faxon, Guy L Richardson, John J Dumphy, Daniel J Ellison, Arthur L Watkins, Robert T Monroe, John Fallon, Roy J Heffernan, Joseph Garland, Leland S McKittrick, Charles F Wilinsky, and Ralph R Stratton

The President, in opening the meeting, announced that the Executive Committee was holding it in lieu of the annual meeting of the Council, the petition to hold the latter meeting having been denied by the Office of Defense Transportation. He said that the personnel of the gathering was made up of the members of the Executive Committee, chairmen of committees and the secretary of the Committee on Public Relations. He suggested that all present be permitted to participate in the discussions attending this meeting and that this privilege be granted by the unanimous consent of the Executive Committee. This consent having been obtained, he invited and urged all present to participate.

He ruled that only members of the Executive Committee would be permitted to vote.

The Secretary announced that the minutes of the meeting of the Executive Committee, held on December 27, 1944, and January 31, 1945, had been sent to each member. He moved their acceptance. This motion was seconded by Dr Frank R

Ober, Suffolk, and it was so ordered by vote of the Committee.

The Secretary offered the record of the Council meeting held on January 31, 1945, as published in the *New England Journal of Medicine*, issue of May 17, 1945. Its acceptance was moved by Dr Edwin D Gardner, Bristol South. This motion was seconded by Dr Eliot Hubbard, Jr, Middlesex South, and it was so ordered by vote of the Committee.

REPORT OF THE TREASURER

This report (Appendix No 1) was offered by Dr Hubbard. He spoke of certain corrections that he wished to make in this report as published in the circular of advance information. He moved the adoption of the report subject to these corrections. This motion was seconded by Dr William H Allen, Bristol North, and it was so ordered by vote of the Committee. (The corrections referred to have been made in the appendix as published.)

REPORTS OF COMMITTEES

Auditing Committee — Dr Z William Colson, Essex North, chairman

This report, which was offered by the chairman, is as follows:

The Auditing Committee appointed the firm of Hartshorn and Walter, accountants and auditors, to audit the books and accounts of the Massachusetts Medical Society. These accountants have submitted an analysis of the revenues and expenses of the Society and a balance sheet of the condition of the Massachusetts Medical Society as of December 31, 1944. The Auditing Committee took cognizance of the fact that these public accountants had been repeatedly chosen in previous years and had executed their functions satisfactorily and that any change in the public accountants would have necessitated a considerable amount of extra work for the Treasurer, which seemed inadvisable in a war year.

The report submitted by Hartshorn and Walter was examined by the Auditing Committee and found to be comparable to those of previous years.

According to the by-laws, the duties of the Auditing Committee include verification of the accountant's examination. No investigation other than an examination of the accountant's report was made, this liberal interpretation of the Auditing Committee's function being consistent with precedent.

(Owing to the need for conserving space because of the shortage of paper, the report of Hartshorn and Walter is not reproduced in the appendices. All significant figures are given in the Treasurer's Report, and detailed information, including the list of securities held, may be obtained from copies of the report on file in the Treasurer's office.)

Dr Peirce H Leavitt, Plymouth, moved the acceptance of the report. This motion was seconded

by Dr Allen, and it was so ordered by vote of the Committee

Committee on Nominations — Dr Ralph R Stratton, Middlesex East, chairman

In reporting for this committee, Dr Stratton presented the following list of officers for the year 1945-1946

President Reginald Fitz, Suffolk
President-Elect Dwight O'Hara, Middlesex South
Vice-President William Jason Mixer, Suffolk
Secretary Michael A Tighe, Middlesex North
Treasurer Elhot Hubbard, Jr, Middlesex South
Assistant Treasurer Norman A Welch, Norfolk
Orator Frank H Lahey, Suffolk

Dr Stratton moved the acceptance of the report. This motion was seconded by Dr William A R Chapin, Hampden, and it was so ordered by vote of the Committee

The President asked if there were any nominations from the floor. There were none

Dr Stratton moved that the nominations be closed. This motion was seconded by Dr. Leavitt and it was so ordered by vote of the Committee

Dr Stratton moved that the Secretary cast one ballot for the slate as submitted by the Committee on Nominations. This motion was seconded by Dr Allen and it was so ordered by vote of the Committee

The President, after announcing that the Secretary had complied with this direction, declared the officers listed above elected

Committee on Membership — Dr Harlan F Newton, Suffolk, chairman

In the absence of the chairman, the report (Appendix No 2) was offered by Dr Leavitt, a member of the Committee on Membership

Dr Leavitt, in submitting the recommendations of his committee, as published in the circular of advance information, said that the committee wished to amend these recommendations by adding the name of Dr Harry H Butler (Norfolk), 48 Winchester Street, Brookline, to those recommended for reinstatement. He moved the adoption of the committee's recommendations as amended. This motion was seconded by Dr Charles J Kickham, Norfolk, and it was so ordered by vote of the Committee

Dr Kickham, at this point, asked permission of the chair to direct certain questions to Dr Leavitt in the latter's capacity as a member of the Committee on Membership. Dr Kickham said he was making the request at the direction of the councilors of the Norfolk District. This permission having been granted by the chair, Dr Kickham addressed the following questions to Dr Leavitt

1 Does the Committee on Membership feel that the local committees on membership are superfluous and that, therefore, it would be wise to have a change in the by-laws whereby the local committees would be omitted entirely?

Dr Leavitt answered, 'By no means'

2 Does Dr Leavitt, as a member of the Committee on Membership, feel that, in the procedure that has been followed to date, all due care has been taken in regard to applicants for membership?

Dr Leavitt replied in the affirmative

Dr Donald Munro, Suffolk, moved that the President appoint a committee to study the by-laws with the end in view of possibly revising the method by which candidates are admitted to membership in the Society. This motion was seconded by Dr Ober

In support of his motion, Dr Munro said that, when the present by-laws were in the stage of discussion, there was considerable debate whether or not it was advisable to give the Committee on Membership the power of vetoing the action of local committees. He added that it was finally decided that it was a good thing to do inasmuch as it would offer protection to local committees and that it was for this reason that certain provisions having to do with the admission of applicants were finally adopted. Dr Munro added that these certain provisions apparently were having some unexpected side effects, which were not anticipated at the time of their adoption

Dr William E Browne, Suffolk, asked how this proposed committee was to be constituted. Dr Munro replied that that should be left to the President

Dr Ober said that local committees should have in their possession the same information about a candidate as is available to the Committee on Membership

Dr Bagnall emphasized what Dr Munro said in respect to the intent of the discussions that preceded and the spirit that prevailed in adopting the present provisions of the by-laws

Dr Munro's motion was adopted by vote of the Committee

At that point in the meeting, no member of the Executive Committee being present from Essex South, the President exercised his prerogative under the by-laws and appointed Dr Walter G Phippen to serve in that capacity

Committee on Arrangements — Dr Roy J Heffernan, Norfolk, chairman

The report, which is as follows, was offered by the chairman

During the fall and winter months, a number of meetings were held to prepare for the 1945 annual meeting. Our aim was to provide a program that would cover the various fields of medicine and surgery, keeping always in mind the needs of the general practitioner. We were extremely fortunate in these busy times in receiving acceptances from many well-known authorities. The prospectus included three representatives from the Surgeon-General's Office and the director of the Army Medical Museum besides physicians from the Mayo Clinic, the Walter Reed Hospital, the University of Michigan and many eminent speakers from our own state

Our sale of booth space again showed an improvement, as \$10,965 worth of space had been reserved by the exhibitors. Of this amount, \$6630 had actually been paid to the treasurer of the Society. Mr. Robert Boyd had excelled his previous excellent record in this department. All the signs and portents indicated that the annual meeting would be one of the best in the history of the Society.

But, as the canny Scottish bard had it, "The best laid schemes o' mice and men gang aft a-gley."

We received a directive from the Office of Defense Transportation dated January 11, soon followed by another dated January 22, 1945. These stated in effect that no meetings or conventions could be held without special permission, if they were attended by more than fifty persons who had to use other than local transportation facilities.

It was obvious from these mandates that we had two courses open to us. One was voluntarily to cancel the meeting, and the second was to apply for permission to hold it. The committee met jointly with the officers of the Society on February 21, 1945, to discuss this matter. At that time we knew that the medical societies of Rhode Island and Delaware had been granted permission to hold their annual meetings.

At this conference the following facts were carefully weighed and considered: the heavy demands on the physicians' time and energy during the war leave very little opportunity for postgraduate study, the global nature of the conflict in which our armed forces are engaged raises the possibility that the returning veteran may introduce diseases unusual to our communities and unfamiliar to the practitioner of medicine, the health of the large number of workers in defense industries in the Commonwealth could be best maintained by physicians well informed in the latest developments in medicine, and the large attendance on the part of medical officers of the military services at previous wartime meetings and the enthusiastic comments of these doctors and their superior officers seemed to indicate that the meeting was of considerable value to them. These and other important considerations convinced the committee that we should apply to the Office of Defense Transportation for permission to hold our meeting as planned.

This application was forwarded to Washington on February 24, 1945. The reply, dated March 9, was received on March 12, and we learned that permission to hold the meeting had been denied.

It was obvious that the committee had no choice but to cancel all arrangements, notify the speakers and return the money to the exhibitors. These actions have now been consummated.

Dr. Heffernan moved the acceptance of the report. This motion was seconded by Dr. Munro, and it was so ordered by vote of the Committee.

Committee on Public Relations—Dr. Albert A. Hornor, Suffolk, secretary.

This report (Appendix No. 3) was offered by Dr. Hornor.

It spoke of a review by the committee of the activities of the Committee on Postwar Planning, as presented by Dr. Howard F. Root, and of the desire of the Committee on Public Relations to support Dr. Root's committee in every way possible.

The work of the Subcommittee on Labor and Industry was reviewed, and the thought expressed that this subcommittee should pursue its activities farther.

The activities of the Subcommittee on Public Information were reviewed, and its recommendations approved.

The report spoke of certain directions that were given to the Subcommittee on Tax-Supported Medical Care and of the approval that had been

given to this subcommittee's work along these lines—with two members of the Committee on Public Relations dissenting in the matter of this approval. The report called attention to the fact that the reports of these three subcommittees would be presented later in the meeting.

The report spoke of a joint program that was about to be entered into by the Red Cross and the Massachusetts Department of Public Health where by the Red Cross would continue to collect blood after the war and turn it over to the Department of Public Health for processing and distribution without charge, in much the same manner as other biologicals are distributed by this department.

Dr. Hornor said that the committee approved of this plan and recommended that the Executive Committee do likewise.

Dr. Hornor moved the acceptance of the report and the adoption of the recommendation contained therein. This motion was seconded by Dr. Frank W. Snow, Essex North, and it was so ordered by vote of the Committee.

Dr. Chapin asked if it was necessary to read reports that were contained in the circular of advance information. The President replied that such reports could be submitted by title only.

Subcommittee on Labor and Industry—Dr. Daniel B. Reardon, Norfolk South, chairman.

This report (Appendix No. 4) was offered by Dr. Reardon. It spoke of certain conferences that had been held by the subcommittee with labor, as represented by the CIO and of the Massachusetts branch of the American Federation of Labor, and with industry, as represented by the Associated Industries. These conferences had to do with the matter of the distribution of medical care. The report summarized the desires of the CIO as being comprehended in the following language: adequate medical care at a price the worker is able to pay. The representatives of the American Federation of Labor believed that their needs could best be met by private insurance carriers, provided the entire cost of such insurance was carried by industry.

The group from the Associated Industries thought that the problem should be defined as twofold: the economic loss to the individual caused by wage stoppage when that individual is ill and the loss due to medical-care costs. This group believed that the first was a social problem, which should be met by legislation. It seemed to be the viewpoint of the industrialists present that industry should not be asked to bear the medical-care costs, beyond certain managerial expenses that might be incidental to any insurance plan set up and paid for by the workers themselves.

Dr. Reardon moved the acceptance of the report.

This motion was seconded by Dr Phippen, and it was so ordered by vote of the Committee

Subcommittee on Public Information—Dr John Fallon, Worcester, chairman

This report, which was offered by the chairman, is as follows

The chief function of your committee has been the organization of the part to be played by the Society in Massachusetts Health Week. Health Week arose from the suggestion of the Massachusetts Dental Society, through its president's assistant, to Governor Tobin that Health Day, normally observed during the first week of May, be elaborated to Health Week. The Governor approved and invited the Massachusetts Medical Society to participate.

The resulting conferences of your committee with His Excellency, the Governor, members of his staff, with officers and representatives of the Massachusetts Dental Society, Massachusetts Hospital Association, Blue Shield, Blue Cross, Blue Triangle, Massachusetts Department of Public Health and Massachusetts Central Health Council and with professional publicists, newspaper men, radio men and officers of this society led to the following commitments

Health Week was advanced from the first to the second week of May (May 6-12) so as to include National Hospital Day (a fixed date, Florence Nightingale's birthday, May 12)

The above-named individuals and agencies severally contributed to Health Week, as a public service and without recompense, fundamental information, elaboration of this into copy for public presentation, newspaper space and radio time

The share of the Massachusetts Medical Society was the furnishing of a list of timely medical subjects and a list of doctors qualified in these subjects for interview by press and radio. From such interviews professional publicists prepared final newspaper and radio copy, subject to editing by this committee. Such copy was distributed to editors and radio stations in each district by the district member of the Committee on Public Relations. As a preliminary step the Massachusetts Medical Society broadcast from a Boston radio station, WORL, on Sunday afternoon, April 22

In its conversations with the public men and publicists named above, your committee made certain observations, which it presents to the Executive Committee

It deduces that the Society should do more than it has in the past to inform the public about medicine and about itself and that it should try to correct certain public misconceptions

It believes that publicity is a technical and specialized field and that it would be more practical for a professional publicist, directed by doctors, to handle the Society's publicity than for a busy doctor to attempt to learn the technique of publicity. It calls attention to the wisdom of a similar course in a similar case: the management of the Society's funds by professional investment counsel

It believes that publicity for many of the health organizations in Massachusetts, foremost of which is this society, might jointly be handled by one central agency. It has appointed a subcommittee to explore this possibility with the Massachusetts Central Health Council

Stories "planted" as news with editors or commentators and therefore subject to editing, may be so changed by the custom of writing for the public taste and by the exigencies of available space and nonmedical editing as to lose point, accent or even truth

Paid-for copy is printed or broadcast unaltered and uncut.

There is ample statistical proof that paid newspaper and radio advertising is the best way of presenting information to the largest number of people. The Blue Shield, Blue Cross and Massachusetts Department of Health have found this true for the kind of information that they furnish the public. Incidentally, the Department of Public Health has found that, of all its methods of bringing information to the public, the method eliciting least response is the pamphlet written and distributed by the department itself

The committee is exploring possibilities of co-operation in the dissemination of health information with agencies such as the New England Council, foundations and so forth. With such conclusions in mind, the committee recommends

1 That the Executive Committee approve payment by the Society for the dissemination of medical information to the public through the medium of newspapers, magazines, radio, cinema or other means

2 That the Executive Committee approve a budget of \$1000 for the Committee on Public Information for administrative expenses

In commenting on this report Dr Fallon said that from the standpoint of getting health information to the public the observance of Health Week could not be considered a success. He pointed out that Germany collapsed the same week and that, as a consequence of this fact, newspaper space and radio time were not so available as they might otherwise have been. He said that one hundred and ten items concerning Health Week did appear in newspapers and that there were four broadcasts. He added that the large amount of material collected under the project as planned need not, however, be lost. It might be used subsequently

Regarding whether or not our Society needs to have its works further publicized, Dr Fallon said his committee believes that this is a subject it should be permitted to investigate further. He said that there seems to be a rather general feeling that the Society's present public relations can be improved on

Dr Fallon said that the following line, which appears in the report, is probably its most important part, "Paid-for copy is printed or broadcast unaltered and uncut," while adding that this was particularly important to the scientifically minded. He said he did not lose sight of the fact that some particular message that the Society might desire to get over to the public by means of paid advertising might need the touch of those more skilled than are physicians in such matters. The final decision of what would appear, however, should rest with the Society

Dr Fallon said that there was ample statistical proof that newspaper and radio advertising is the best way of presenting information to the largest number of people. He added that this was the experience of the Blue Shield, Blue Cross and the Massachusetts Department of Public Health

He spoke of a radio program initiated by the Michigan State Medical Society, in which program this society had invited us, together with sixteen other states, to participate. He referred to a sample recording of the program that the committee heard, and added that the members of the committee considered it a "little too blunt for their palates"

Dr Fallon moved the acceptance of the report and the adoption of the recommendations contained therein. This motion was seconded by Dr Peirce Leavitt

Dr Reardon said that newspaper and radio

publicity were expensive procedures. He asked Dr. Fallon if his committee had any idea concerning the amount of money the Society should appropriate every year for this purpose.

Dr. Fallon, in replying to Dr. Reardon, said he was in agreement with the latter that this type of publicity was expensive. He added, however, that the moneys asked for in the committee's second recommendation were not to be spent in publicity but rather for the purpose of enabling the committee further to study public-relations methods. Paid space might not often be needed, but he thought it advisable to have the Executive Committee pass on the principle involved.

Dr. Hornor asked if the Society's present tax-exempt status would be affected by engaging in such activities. Dr. Fallon replied that this phase of the subject had been discussed with Mr. Robert G. Dodge, attorney.

He read the following excerpt from a letter from Mr. Dodge:

I see no grounds on which the Massachusetts Medical Society could by advertising of any kind lose its exemption from income taxation.

Even if you should advertise, for example, a statement of the position of the Society with regard to the Wagner Act, that would make no difference, so far as taxation is concerned.

Dr. Browne said that, if and when the Society is finally committed to the policies outlined by the committee, it should spend sufficient moneys to do the job properly.

Dr. Fallon's motion to accept the report and approve the recommendations was adopted by vote of the Committee.

The Committee recessed at 1:00 p.m. and reconvened at 1:45 p.m.

Dr. Bagnall read the President's Report on the State of the Society. (This report is published in full elsewhere in this issue of the *Journal*.) At its conclusion, Dr. Bagnall was greeted with loud applause.

Committee on Tax-Supported Medical Care — Dr. John J. Dumphy, Worcester, chairman.

This report, which was presented by the chairman, is as follows:

The Committee on Tax-Supported Medical Care met with the Commissioner of Public Welfare, Mr. Arthur Rotch, on April 18, 1945.

Two subjects were taken up — first, the payment of physicians caring for welfare patients in unstaffed hospitals, and, second, the payment of physicians taking care of all welfare patients.

With regard to the first question, Mr. Rotch stated that he is prepared to recommend payment of present Blue Shield rates for surgical patients cared for by physicians in unstaffed hospitals. For medical cases, the payment would be four dollars for the first day and two dollars per day thereafter for a period not to exceed two months or one hundred and fifty dollars. For illness longer than two months requiring hospital care, each case would be considered separately.

With regard to the question of payment of physicians on all welfare patients, Mr. Rotch stated that, under the

present system of medical practice whereby free services are available, as the state commissioner, he must avail himself and the Commonwealth of free services where they are available.

The committee recommends that the Council approve the policy of paying physicians in unstaffed hospitals for the care of welfare patients at the following rates for medical cases, four dollars for the first day and two dollars for each succeeding day for a period not to exceed two months or a total of one hundred and fifty dollars, and for surgical cases, the present Blue Shield rates prevail. For welfare patients in staffed hospitals that they continue to be cared for as staff patients without charge by attending staff physicians.

In commenting on the report Dr. Dumphy said that Mr. Ray Long, Commissioner of Veterans and Pensions, was much disturbed by the great variation in doctors' bills for handling the same type of service and that the latter had asked that the Blue Shield rates be made the standard for payment of surgical fees. He said his committee was in agreement with Mr. Long on this proposition. He referred to that part of the report of the Committee on Public Relations which directed his subcommittee to approach Mr. Rotch, Commissioner of Welfare, and ascertain from the latter whether or not he, too, would be willing to accept the Blue Shield rates as the standard for the payment of surgical fees for services rendered to welfare cases in unstaffed hospitals. Dr. Dumphy explained that at the time his subcommittee received this directive from the Committee on Public Relations, an agreement had been entered into whereby the Welfare Department would pay three quarters of the rates established by the Blue Shield schedules for surgical services rendered such cases. He added that Mr. Rotch had accepted this latest proposition and he referred to a letter that he had received from him, a copy of which was in the possession of each member of the Executive Committee.

Dr. Dumphy then referred to a further directive that his subcommittee had received from the Committee on Public Relations, namely, that the Commissioner of Welfare should be approached with the end in view that these same regulations should equally apply to staffed hospitals. To this proposition Dr. Dumphy said Mr. Rotch could not agree.

Dr. Dumphy now moved the acceptance of the report and the adoption of the recommendation contained in its last paragraph. This motion was seconded by Dr. Munro and it was so ordered by vote of the Committee.

(For schedule of fees under this heading, refer to Appendix No. 5.)

At that point in the meeting Dr. Bagnall spoke of a visit that he made to Michigan on April 27 and 28, 1945. He said he made the visit in consequence of an invitation issued to him and to the presidents of several other state medical societies by the president of the Michigan State Medical Society.

The following resolution was adopted by this group so gathered:

BE IT RESOLVED, That this group expresses its continued loyalty to the American Medical Association, That it is the duty of the various state medical societies to advise the American Medical Association through its Council on Medical Service and Public Relations, of their wishes in regard to national health legislation, That the presidents of the several states and District of Columbia medical societies or their representatives act as a permanent committee immediately to set up drafting panels in each state for this purpose, That states not represented here today be invited and encouraged to join in this work, and That the president of the Michigan State Medical Society be designated as temporary chairman of this committee to facilitate its activities

A second resolution, which is as follows, was also adopted

BE IT RESOLVED, That the president of the Michigan State Medical Society be authorized to appoint a committee to study the feasibility of commercial radio broadcasting as related to the various states here represented in co-ordinating and co-operating in the development of such programs as presented today (April 27) and to make recommendations for the best manner of carrying out such a program

Dr Bagnall said that Dr E J McCormick of Toledo, a member of the Council on Medical Care and Public Relations of the American Medical Association, and the secretary of that council were present at the meeting and that they together with the 18 states represented unanimously approved the resolutions

In referring particularly to the planning committees mentioned in the first resolution Dr Bagnall said that these committees should consider what might be strategic and desirable in the way of legislation to put before Congress, that their plans will then be processed through a central committee, elected from these eighteen states and from any other state that might care to come into the plan, and that the agreed-on action be then processed through the Council on Medical Service and Public Relations of the American Medical Association for reference to the House of Delegates of the American Medical Association Dr Bagnall suggested that the Committee on Public Relations of the Massachusetts Medical Society might be designated as the planning committee under this title It was so moved by Dr Kickham This motion was seconded by Dr I S F Dodd, Berkshire

Dr Hornor asked for a definition of panel planning Dr Bagnall said that there were many influential people who believe that some legislation relating to medical care will come out of Congress before many years and that the medical societies should have a share in planning it He added that the purpose of the panel planning committee was to bring the thinking of the several states to the attention of the Council on Medical Care and Public Relations of the American Medical Association

Dr Kickham's motion was adopted by vote of the Committee

Committee on Legislation — Dr William E Browne, Suffolk, chairman

This report (Appendix No 6) was presented by the chairman who moved its approval This motion was seconded by a member of the Committee

Dr Reardon asked if he had correctly heard Dr Browne say that under one of these bills an osteopathic diplomate would have the privilege of practicing medicine in Massachusetts without taking the examinations of the Board of Registration in Medicine Dr Browne replied in the affirmative saying that such a person would have the privilege of practicing medicine in Massachusetts provided he holds a certificate from the national osteopathic examiners, provided he is a graduate of a recognized school of osteopathy, provided his school is approved by the Massachusetts Approving Authority, provided he presents himself to the Massachusetts Board of Registration in Medicine, and provided that this latter board may, in its discretion, grant him a license to practice medicine He added that there are six recognized schools of osteopathy in the country

In answer to a question by Dr Hornor, Dr Browne said that the practice of medicine had never been defined by the Massachusetts Laws

Dr Kickham said he had been requested by the Norfolk District Medical Society to ask on what grounds the so-called "reportable cancer bill" had been approved by the Committee on Legislation He added that as his district had the facts this bill not only served no good purpose but might do much harm

Dr Browne replied that this bill had been discussed in the Council meeting held on January 31, 1945, and that he said, at that time, that although his committee had not had sufficient time to really study this bill, it probably would approve it in principle and that there was no remonstrance As time went on, he added, it became apparent that those who knew much about cancer favored the bill, finally, he said that this bill had been considered by the Executive Committee of the Committee on Legislation several days previously and that no opposition to it was apparent at that time He pointed out that the representative from the Norfolk District Society sat in this meeting Dr Humphrey McCarthy, Norfolk, said that he did present Norfolk's attitude toward this proposed legislation at the meeting referred to by Dr Browne and that nobody else present opposed the legislation

Dr Browne's motion to approve the report was so ordered by vote of the Committee

Committee on Information Bureau — Dr Walter G Phippen, Essex South, chairman

This report, which was offered by the chairman is as follows

Since the last meeting of the Council the Bureau of Information has continued to function and grow. Our mailing list for the *Bulletin* has grown from 175 to 194. The number of requests for information over the phone or by letter during the period from January 23 to March 1, has been 96 compared with 75 over the longer period before. These requests were almost all for information concerning operations or for the *Bulletin*. There have also been over 30 requests for various information, such as refresher courses, and so forth, by persons at the office. Since the last report also we have added the Boston Dispensary to our list of hospitals sending us daily information, bringing the number up to twenty-two, including the Lahey Clinic. As this is the number we originally planned to cover, we are quite satisfied.

The committee believes that the Bureau is now well organized and working satisfactorily and that its future development will be very much a part of the postwar planning activities of the Society, it therefore recommends that this committee be discharged and that the Bureau be transferred to the Subcommittee on Postgraduate Education.

Dr Phippen moved the acceptance of the report and the adoption of the recommendation contained therein. This motion was seconded by Dr Leavitt, and it was so ordered by vote of the Committee.

Committee on Postwar Planning — Dr Howard F Root, Suffolk, chairman

This report (Appendix No 7) was offered by the chairman. It spoke of the result of a questionnaire that had been sent to doctors in the armed services concerning their future educational needs. The emphasis placed by the doctor, particularly in the younger group, was on the necessity of additional clinical training. The report went on to say that at least 12,000 hospital residencies in this country must be available if the needs of the returning doctor are to be met. The report continued to say that half this number are now available and that if the need is to be met, hospitals that have never had residencies must establish them.

The following two paragraphs are quoted from the report:

The returns from this questionnaire indicate how fully the recent graduate in medicine appreciates the inadequacy of his training, particularly along clinical lines. It is not sufficient to dismiss this as one of the exigencies of the war. If the same high standards of medical care to which the American people have been accustomed are to be maintained, notice must be taken of the inadequacy in preparation which looms large in the doctor trained in wartime, and every effort bent toward its relief.

The Postwar Planning Committee of the Massachusetts Medical Society believes that the hospitals of the Commonwealth can and should play a most important part in any program directed toward that end.

Dr Root spoke of the steps that the Subcommittee on Hospitals was taking to acquaint hospitals of Massachusetts with their opportunities along these lines. He added that on June 20, 1945, under the auspices of this subcommittee, a meeting was to be held with hospital representatives for this purpose. The report spoke of the interest that many doctors in the service showed in industrial medicine. The report called for an expansion of the Bureau of Information.

The report emphasized the necessity of the Society's being able and ready to assist the returned doctor in his relocation problems, and in respect to this Dr Root urged the district societies to return completed the questionnaire sent out by the Bureau of Information of the American Medical Association.

Dr Phippen moved the acceptance of the report. This motion was seconded by Dr C Bertram Gay, Worcester North.

At this point, the Secretary said that twelve of the districts (Barnstable, Berkshire, Bristol North, Essex North, Hampden, Hampshire, Middlesex North, Norfolk, Norfolk South, Plymouth, Suffolk and Worcester) had returned completed the questionnaire referred to by Dr Root. He urged the other districts to take this matter very much to heart.

Dr Phippen's motion was adopted by vote of the Committee.

Committee on Ethics and Discipline — Dr Ralph R Stratton, Middlesex East, chairman

The report (Appendix No 8) was offered by the chairman, who moved its acceptance. This motion was seconded by Dr Chapin.

In commenting on the report, Dr Stratton spoke of how time-consuming was the work of his committee, of the pains that had to be taken in the presentation of cases, of interviews that had to be held, of letters that had to be written and of files that had to be consulted.

In speaking of the last case mentioned in the report, he said that, although the offense was serious, the accused, who was found guilty, was let off with a severe admonition by the President, the committee taking note of the fact that this was the first time this physician had been before it. The motion to accept the report was adopted by vote of the Committee.

Committee on Medical Defense — Dr Arthur W Allen, Suffolk, chairman

This report, which is as follows, was offered by Dr Edwin D Gardner, Bristol South, in the absence of Dr Allen.

At this time, we have eleven cases pending trial. During the past year, three cases have been disposed of satisfactorily. We have acquired four new cases during the year.

Most of these suits are brought on very little evidence of malpractice and for this reason a judgment is rarely given against our fellows. Many of the suits never come to trial. There are, however, necessary legal expenses associated with these cases, the total bill for legal services during the year 1944 being \$853.03.

Dr Gardner moved the acceptance of the report. This motion was seconded by Dr C Bertram Gay, and it was so ordered by vote of the Committee.

War Participation Committee — Dr Guv L Richardson, Essex North, chairman

The report, which is as follows, was offered by the chairman

Since the last Council meeting, the activities of this committee have been concerned with assisting the Office of Price Administration in their relations with physicians. So far as we can determine, controversial matters have been adjusted satisfactorily to all concerned. The OPA asked that three additional local medical advisory committees be appointed, one for Lowell, one for Quincy and one for Holyoke. The committee in Lowell, under the chairmanship of Dr Daniel J Ellison, has already been set up. The others are in the process.

Dr Richardson moved the acceptance of the report. This motion was seconded by Dr W H Allen, and it was so ordered by vote of the Committee.

Medical Advisory Committee to the Regional OPA — Dr Joseph Garland, Suffolk, chairman

This report, which is as follows, was offered in the absence of Dr Garland by the Secretary

The duties of this committee have not abated since its last report and perplexing problems continue to present themselves. These are augmented by the fact that stricter rationing has been necessary this spring and will presumably last for an indefinite period, and the number of applications for increased rations is steadily increasing.

It seems still apparent that many physicians have not availed themselves of the opportunities offered to understand the rationing problem and to co-operate in the attempts that are being made to solve it. Valuable assistance continues to be given in selected communities by the local war-participation committees, acting as medical advisory committees.

The Secretary moved its acceptance. This motion was seconded by Dr Gardner, and it was so ordered by vote of the Committee.

Committee on Society Headquarters — Dr Frank R Ober, Suffolk, chairman

The report, which was offered by Dr Ober, outlined two plans by which the headquarters might be improved to serve better the purposes of the Society. Although the discussion indicated that the Committee favored Plan Two rather than Plan One, it was the consensus that more detail should be supplied by the Committee on Headquarters before any final action was taken.

It was moved by Dr Phippen and seconded by Dr Munro that the Committee tentatively approve Plan Two and direct the Committee on Society Headquarters to secure such options as are necessary for its realization. This motion was adopted by vote of the Committee.

Committee on Medical Education — Dr Robert T Monroe, chairman

In the absence of Dr Monroe, the Secretary offered the following report, which had been prepared by the former

At the request of the secretary of the Society, our committee has considered the problem arising under the G I Bill of Rights in regard to postwar training of veterans in the healing arts. The former expressed the fear that, unless our committee gave this matter some attention, the veteran might not receive in quality the training to which he was entitled.

The committee found that the Veterans' Bureau has no choice but to accept the list of schools for the training of veterans in the healing arts, under the G I Bill of Rights, supplied by the Board of Collegiate Authority of the Massachusetts Department of Education.

The committee chairman met with Mr F G Nichols, of the Board of Collegiate Authority, Mr Herbert A Dallas, of the State Division of Vocational Rehabilitation, and Dr Joseph H Shortell, chairman of the Massachusetts Medical Society's Committee on Rehabilitation. The committee has offered its services to Mr Nichols in advising him as to the qualifications of schools of medicine, nursing, physiotherapy, laboratory technicians, x-ray technicians and so forth. This offer has been accepted.

It may be desirable also for us to offer to veterans, through the Veterans Administration, information and advice regarding the various training schools and what they train for.

We shall print a list of approved educational institutions in the *Journal* from time to time, with the permission of Mr Nichols.

The Secretary complimented the committee on its efforts, and described the job done by it as bound to redound to the advantage of the veteran in the latter's search for education in the healing arts under the G I Bill of Rights.

The Secretary moved the acceptance of the report. This motion was seconded by a member, and it was so ordered by vote of the Committee.

Committee on Physical Therapy — Dr Arthur L Watkins, Middlesex South, chairman

The following report was offered by the chairman.

The purpose of this committee has been to acquaint and educate the general practitioner with the use of those physical therapeutic measures that are of value in medical practice. With this end in view an article, "Physical Medicine in Rehabilitation," was published in the February 15 issue of the *Journal*. During the past few years the interest of physicians specializing in physical therapy has been broadened to also include occupational therapy, and the name physical medicine has been generally used to indicate both physical and occupational therapy, and the use of physical agents in diagnosis and for the prevention of disease.

It is accordingly recommended that the activities of this committee be enlarged to include occupational therapy in its relation to medical practice and that the name of the committee be changed to the Committee on Physical Medicine.

Dr Leavitt moved the acceptance of the report and the adoption of the recommendations. This motion was seconded by Dr Gardner, and it was so ordered by vote of the Committee.

Committee on Rehabilitation — Dr Joseph H Shortell, Suffolk, chairman

In the absence of Dr Shortell, the Secretary said that it was expected that a report from this committee would be available for discussion at this meeting. He added that the report had not been received. For the information of the Committee, he said that the report, when received, would deal with a fee schedule that the Massachusetts Department of Rehabilitation sought to have set up in dealing with payments for medical services rendered to those of our people whose disabilities were static and remediable.

He said that if the individual were to profit under this program, actual indigence need not be shown. Such an individual, however, must show that he is unable through his own efforts to meet the costs of his rehabilitation. He added that a hernia that was impairing an individual's ability to follow a gainful occupation would be regarded, under this program, as a disability that was static and remediable.

Committee on Industrial Health — Dr Dwight O'Hara, Middlesex South, chairman

This report, which was offered by the chairman, is as follows:

During the past year, the Committee on Industrial Health has met as a whole four times, its subcommittees have met oftener. Among the subjects discussed at some length were rehabilitation in industry, aluminum therapy and prophylaxis for silicosis, various types of programs for postgraduate education, sarcoid-like reactions to chemical irritants and the merits of bills dealing with industrial health before the current sessions of the Legislature. With the approval of the Committee on Legislation we expressed ourselves in writing concerning these legislative matters to the proper state authorities. The committee co-operated with the War Participation Committee in emphasizing the responsibilities of doctors in the control of industrial absenteeism, and has continued to furnish editorial material which has been cordially accepted by the editor of the *Journal*. During the year, the committee has continued its discussions of industrial health in the small manufacturing plants of the Commonwealth. It has formulated its ideas on this subject to some extent, and would ordinarily embody them in this report. The fact that the annual report could not be presented to the Council as a whole, however, led us to publish this material in the April 5 issue of the *Journal* under the title "A Statement Concerning Industrial Hygiene in the Small Plants of Massachusetts." Your committee considers this statement to be its main contribution for the year.

The committee has from time to time aided industrial plants by making medical contacts for them, and has succeeded in placing a few physicians in industrial positions. Members of the committee have visited industrial plants in several parts of the Commonwealth on the invitation of their managements. The committee had planned for and hoped for larger participation in the program of the annual meeting of the Society, and had tentatively arranged for doctors to visit one of the large shipbuilding plants in Boston in connection with the meeting this year. A subcommittee was already in action in these matters when it became known that the meeting for 1945 was cancelled.

On May 8, under the auspices of the Hampden District Medical Society and the Springfield Academy of Medicine, the committee presented four speakers in an afternoon-and-evening program in Springfield. The papers were

arranged particularly to interest the general practitioner, and were well received, although they did not attempt to reproduce in volume the programs held in Boston in 1942 and 1943.

Dr O'Hara moved the acceptance of the report. This motion was seconded by Dr W H Allen, and it was so ordered by vote of the Committee.

Committee Appointed to Make Recommendations as to the Choice of Future Directors of the Blue Shield — Dr Leland S McKittrick, Suffolk, chairman

This report, which in the absence of the chairman was offered by the Secretary, is as follows:

The committee met at 8 Fenway on April 18, 1945. The committee was fully represented except for Dr Peirce H. Leavitt, who was out of the city and not available. In addition to the members of the committee, Dr Elmer S Bagnall and Dr Reginald Fitz were present.

It was voted to recommend to the Corporation the appointment of the following five men to replace those whose term of office ends this year:

Mr Oliver G Pratt — Reappointment
Mr Thomas G Brown — Reappointment
Dr Elmer S Bagnall — To replace Dr Mongan
Mr Ernest Johnson — Reappointment
Mr Daniel Boyle — Reappointment

The attendance record of the present Board of Directors was reviewed, and it was voted to recommend that Dr Frank R Ober, whose office expires in 1947, be asked to resign and that Dr Arthur W Allen, 266 Beacon Street, Boston, be elected to fill his place.

The President observed that he was not present when the above recommendations were made.

Dr Ober said that he had missed two or three meetings of the Board of Directors of the Blue Shield because the meetings were not always held as originally scheduled and that on those occasions he had made arrangements to be elsewhere when these meetings were finally held.

Dr Munro moved the acceptance of the report. This motion was seconded by Dr W H Allen.

Dr Bagnall explained that the Committee had been appointed because it seemed desirable to have a group of men who were sitting in continuity, and thinking at the time about the directorate in terms of the needs of the Blue Shield.

Dr Reardon asked if he had understood it correctly that Dr Mongan's name had been dropped from the list. The president replied in the affirmative.

Dr Reardon asked if Dr Mongan had been consulted and if there was any reason given for dropping him. The President replied he did not know, repeating that he was not present when the selections were made.

Dr Reardon said that it seemed to him that Dr Mongan is a man who deserves every consideration from the Society and from every fellow of the Society. He added:

He has been a tireless worker, giving time and energy and every effort for the benefit of the Society, and I should think it would be only a matter of courtesy to him to ask him if he did not want to serve any longer, if so, that would be the time to drop him.

I do not believe that a man who has given such service as he has given to the Society should be dropped without an adequate excuse

I am not a member of the Committee, and I am not speaking as a member of the Committee, but I do think that he is such a valuable man to the Society that he should be retained on the Board. Personally, I should like to see his name still go down on that list of names suggested

The President said he was not seeking any office, that he was a bit tired and that instead of desiring to take on a new job, he would like to be relieved of some he already had

Dr Fitz said that it was his recollection that Dr Mongan had finished his term. The President confirmed this

Dr O'Hara said that he shared everybody's feeling toward Dr Mongan but that this was a replacement at a perfectly natural time and that nobody should take umbrage at it

Dr Munro said that he was present at the meeting of the committee and that much time had been spent in canvassing the situation. He added that the committee had available for its use information that is not available to the Executive Committee, relative to plans, policies, financial conditions, financial commitments and out-of-state relations of the Blue Cross and Blue Shield, and that the deliberations were conducted in a spirit of friendliness to all, with the welfare of the Blue Shield the paramount issue

The report was accepted by vote of the Committee

Committee on Postwar Loan Fund—Dr George Leonard Schadt, Hampden, chairman

The report, which is as follows, was offered by the chairman

The Committee on Postwar Loan Fund, at a meeting held on May 2, 1945, decided that the time has now arrived to set up a postwar loan fund. It therefore recommends that

- (1) A sum of not more than \$25,000 of the Society's funds be drawn on for this purpose
- (2) That the President be empowered to appoint a committee of five, to include the treasurer and secretary of the Society and the present chairman of the Committee on Postwar Loan Fund, to administer this fund in accordance with the recommendations made by this committee in the report presented on May 22, 1944 as follows
- (3) That the amount of loan granted be left to the discretion of the board or committee appointed by the President
- (4) That just enough interest be charged—not to exceed 2 per cent—to cover carrying charges and remind the member obtaining a loan of his obligation
- (5) That no endorsers be required
- (6) That loans shall be limited to a period of twelve months subject to renewal at the discretion of the board or committee appointed
- (7) That only those who were members, in good standing of the Massachusetts Medical Society on the date they entered the armed forces shall be permitted to borrow from this fund

(8) That, to inform members of the Society in the armed forces of the availability of this fund, information be printed in the *New England Journal of Medicine*. There shall also appear in a box on the cover of the *Journal* an announcement calling attention of the members to the article on the inside page

(9) That form letters shall be sent to the members in the armed forces notifying them of the existence of this fund

(10) That form letters shall be sent out to the other members of the Society with the annual bills for dues bringing to their attention the existence of this fund and its purpose

(11) That the fund shall be administered from the headquarters of the Massachusetts Medical Society

Dr Schadt announced that the recommendations contained in the report had the approval of the Committee on Finance

He moved the acceptance of the report. This motion was seconded by Dr Leavitt, and it was so ordered by vote of the Committee

Dr Schadt moved the adoption of the first recommendation. This motion was seconded by Dr Chapin. With regard to the personnel setup under the recommendation, Dr Schadt said that he was in agreement with those who criticized this on the basis that it usurped the President's prerogative. He added that he had no particular desire to serve on the committee, but that he would do so if he were appointed. The recommendation was adopted by vote of the Committee

Recommendations 2, 3, 4, and 5 were adopted by vote of the Committee without debate. Dr Schadt moved the adoption of the sixth recommendation. This motion was seconded by Dr Leavitt. After considerable debate, which had principally to do with the question of enlarging the numbers who might be permitted to participate in the plan, it was voted by the Committee to adopt the recommendation as originally offered. Recommendations 7, 8, 9, 10, and 11 were severally moved by Dr Schadt for adoption. These motions were seconded, and they were so ordered by vote of the Committee

NEW BUSINESS

The Secretary was in the receipt of the following communication

Dr Michael A Tighe, Secretary
Massachusetts Medical Society
Boston, Massachusetts

Dear Dr Tighe

On February 16 Dr Bagnall submitted to me a letter which he had received from W. L. Bell & Co., an insurance management corporation. The substance of this letter was a request that the Massachusetts Medical Society approve an accident and health cash indemnity policy of the National Casualty Company of Detroit, Michigan. Mr. Bell stated in his letter that this was a group type of policy in which his corporation was endeavoring to interest such societies as the Massachusetts Medical Society and its county divisions as well as local medical societies, and such organizations as the Massachusetts Bar Association. This plan if subscribed to in groups, would allow the premium to be at a comparatively low rate.

Dr Bagnall, in submitting it to me, suggested that I review the proposition and judge as to its merits for the Massachusetts Medical Society.

In the furtherance of Dr Bagnall's request I did review the data submitted and also had Mr Bell submit the names of any organizations in the Commonwealth who are interested in this proposition. Also, there was submitted a sample copy of the insurance contract.

After careful review of the entire matter I feel that there is certain merit to this type of group cash indemnity policy and that possibly certain members of our organization might wish to avail themselves of the reduced premium payments which would be available. It is my understanding that such a plan as submitted by Mr Bell would require fifty per cent of our membership participating before such premium reduction would be available.

Any plan for the insurance of our membership necessarily merits careful study and analysis, both pro and con. Such a plan also needs careful consideration, not only of the financial stability of the parent company but also of their local representatives. The results that have been obtained where the plan is already in existence need study in order to evaluate the proposition. Therefore, I recommend that the Executive Committee of the Council of the Massachusetts Medical Society allow the matter to be presented to them for consideration, and if deemed advisable, that a committee of three be appointed by the president of the Massachusetts Medical Society to study the matter and bring specific recommendation to the attention of the Executive Committee at a future meeting.

I submit a resolution in order to bring this formally before the Executive Committee.

Yours very sincerely,

(Signed) CHARLES J KICKHAM

Dr Kickham moved that the president appoint a committee of five to study the plan for a group accident and health insurance policy. This motion was seconded by Dr Leavitt.

Dr Kickham said that his investigations showed that eleven of the eighteen districts were now covered by one insurance company. He added that the Norfolk District had had this matter under investigation for some time and that there seemed to be a demand in that district for this type of insurance.

Dr Phippen said that inasmuch as eleven of the district societies had already entered this field on their own, and were satisfied, it might be well to leave the matter of what the other districts would do in their own hands. Dr Reardon and Dr W F Ryan, Middlesex North, expressed a like view.

Dr Kickham's motion was defeated by vote of the Committee.

At that point, the President read a telegram from Chicago that announced that on the next day, Senator Robert F Wagner, of New York, would submit a revised Wagner Bill.

Dr Dwight O'Hara, Middlesex South, introduced the following amendment to the by-laws:

The by-laws of the Massachusetts Medical Society are hereby amended by adding a new chapter, to be known as Chapter X. This chapter shall read as follows: Any provision or provisions of these by-laws may be temporarily waived, provided such waiver is not in conflict with the laws of the Commonwealth, provided the provision or provisions sought to be waived be clearly designated,

provided the period during which such waived provision or provisions are to continue be definitely stated, provided notice of the proposed waiver accompany the call of the annual meeting and provided the members present at such an annual meeting unanimously consent.

Dr O'Hara moved the approval of the amendment. This motion was seconded by Dr Leavitt.

Dr O'Hara explained that as the by-laws now stand none of its provisions could be waived and that circumstances might arise in the future that might make such an act desirable.

Dr O'Hara's motion to approve the amendment was so ordered by vote of the Committee (The amendment will go to the annual meeting of the Society in 1946 for rejection or adoption).

The President read the following obituaries:

Dr John C V Fisher, of West Roxbury, died February 20. He was in his fifty-third year.

He received his degree from Boston University School of Medicine in 1917. He served as a surgeon for the United States Merchant Marine during the first world war. He had practiced in Boston since 1919 and had been obstetrician at the Massachusetts Memorial Hospitals since 1928. He was associate professor of obstetrics at Boston University School of Medicine. He was a fellow of the American College of Surgeons, and a member of the New England Obstetrical and Gynecological Society.

Dr Fisher was president of the Norfolk District Medical Society from 1943 to 1944 and had been a member of the Council of the Massachusetts Medical Society for several years.

His widow and a brother survive.

Dr Edwin R Leib, of Worcester, died May 3. He was in his seventy-first year.

He received his degree from Boston University School of Medicine in 1899. He retired as chief of the medical service at Hahnemann Hospital a few months ago but remained on the staff as a consultant. He was also a consultant on the Belmont Hospital staff. Dr Leib had served as epidemiologist in the Worcester Health Department for more than thirty years. He was president of the Worcester Blood Bank.

His memberships included the Worcester District Medical Society of which he was a past president, as well as a councilor at the time of his death. He was a fellow of the American Medical Association.

His widow and a brother survive.

At the direction of the President, the Committee stood for one minute in silent tribute to the memory of these deceased councilors.

The Secretary submitted the following changes in membership:

Membership as of May 23, 1944

<i>Losses</i>	
Deaths	100
Resignations	11
Deprivations	16
Total	127

<i>Gains</i>	
New fellows	119
Reinstatements	11
Total	130
<i>Net Gain</i>	3

Membership as of May 23, 1945

5783

5786

The President submitted the following list of ad interim appointments

To the Council Dr Louis A Sieracki, Norfolk, to replace Dr J C V Fisher, deceased Dr Philip E Meltzer, Suffolk, to replace Dr George B Fenwick, deceased

To the Section of Anesthesiology Dr Sidney C Wiggin, chairman, and Dr Leo V Hand, secretary

To the Committee on Legislation Dr Curtus C Tripp, representing Bristol South, to take the place of Dr Edwin D Gardner, resigned

To the Committee on Public Relations Dr Milton J Quinn, representing Middlesex East, to take the place of Dr J Harper Blaisdell, deceased

To the Subcommittee on Public Information of the Committee on Public Relations Drs John Fallon, chairman, Michael A Tighe, Richard M Smith, Ralph R Stratton, Roy J Ward, Roger T Doyle, Roy J Heffernan and Howard F Root

To the Subcommittee on Labor and Industry of the Committee on Public Relations Dr Daniel B Reardon, chairman, George J Connor, Daniel J Ellison, John Fallon and Michael A. Tighe

To the Subcommittee on Hospitals of the Committee on Postwar Planning Dr Clifton T Perkins

To the Subcommittee on Organization of the Committee on Postwar Planning Dr Charles E Mongan

To the Subcommittee on Postgraduate Education of the Committee on Postwar Planning Drs Harry C Solomon and Charles G Mixer

To the Committee to Make Recommendations as to the Choice of Future Directors of the Blue Shield Drs Leland S McKittrick, chairman (term expires May, 1949), George G Smith (term expires May, 1948), Elliott P Joslin (term expires May, 1947), Donald Munro (term expires May, 1946) and Peirce H Leavitt (term expires May, 1945)

These appointments were confirmed by vote of the Committee

At that point the President introduced Dr Reginald Fitz, president of the Massachusetts Medical Society for the year 1945-1946. He was greeted with loud applause

Dr Fitz submitted a list of nominations to standing committees. He moved the approval of these nominations. This motion was seconded by Dr Munro, and it was so ordered by vote of the Committee. Dr Fitz then read a list of nominations to special committees and subcommittees. He moved the approval of the nominations. This motion was seconded by Dr O'Hara, and it was so ordered by vote of the Committee. (The members of the standing and special committees for the year 1945-1946 appear elsewhere in this report.)

The President read the following communication from Dr John F Kenney, president of the Rhode Island Medical Society

Dr E S Bagnall, *President*
Massachusetts Medical Society
Groveland, Massachusetts

Dear Dr Bagnall

At the meeting of the House of Delegates of the Rhode Island Medical Society held on May 9, the House voted unanimously that the Rhode Island Medical Society should take leadership at the present time in forming a New England Medical Council of the medical societies for the purpose of discussing mutual problems

A year ago it was proposed by the Rhode Island Medical Society that such a council be activated and an attempt was made to interest the other New England societies. We now hope that this plan may be realized and we are confident that it would be most advantageous to all of us in finding ways in which to solve both local and national problems that directly concern the practice of medicine and the provision of medical and health services to the peoples in our states

I enclose a copy of the proposal as tentatively advanced last year to give you an idea of how such a council might possibly be organized and made workable

We shall appreciate your kindness in bringing this matter before your policy-making body, and I shall hope to hear from you in the near future relative to the decision of your society

When we have heard from you we shall be in a better position to set a definite date when a conference might be held here in Providence to formulate details

(Signed) JOHN F KENNEY, M D

May 19, 1945

The proposal referred to in the letter appears as Appendix No 9

Dr Leavitt moved that the Society participate in the plan proposed by Dr Kenney. This motion was seconded by Dr Munro, and it was so ordered by vote of the Committee

Dr Leavitt addressed the chair and said that he wished to express his approval of the way in which Dr Bagnall had run things during the year. "You have been fair," he added, "in a trying job, and I want personally to thank you for a job wonderfully well done"

There being no further business before the meeting at 5 20 p m, the President declared the meeting adjourned

MICHAEL A TIGHE, *Secretary*

APPENDIX NO 1

TREASURER'S REPORT

During 1944 income from dues was further reduced owing to more members being in the service with dues remitted — \$39,723 in 1944 as compared with \$43,390 in 1943. Non-resident dues dropped from \$1651 to \$1492 during the same period

Income from investments in the General Fund rose from \$3466 in 1943 to \$3969 in 1944, and from investments in the Building Fund from \$1776 in 1943 to \$1960 in 1944. An outstanding achievement was the increased income from the annual meeting contributed by the Committee on Arrangements and in large part due to the efforts of the Executive Secretary, \$3495 in 1944 as against \$1750 in 1943

The yield from securities held in the General Fund increased during the year from 2.40 to 2.43 per cent, and from those held in the Building Fund from 2.95 to 3.14 per cent.

Total value of the securities in the General Fund stands at \$167,614 book value and \$170,885 market value, an increase during the year of \$7056 and \$9838 respectively. Correspondingly in the Building Fund book value of holdings stands at \$68,170 and market value at \$70,858, an increase of \$5721 and \$5284 respectively

Changes in the portfolios of the two funds have largely been replacements of bonds matured or called by bonds of similar character, government issues and a slight increase in preferred stocks

Ten thousand dollars (\$10,000) in Commonwealth of Massachusetts 3½ per cent bonds held in the Phillips Fund matured and were replaced by an equal amount in United States War Savings Series G bonds. Including these, the Society has increased its government bond holdings by \$22,000, this year, to a total of \$96,000

According to the vote of the Council in June, 1929, providing that interest received from the Building Fund principal could be applied toward the expenses of maintenance of society headquarters, this action has been followed and such income has not been added to the Building Fund total.

One thousand, one hundred and sixty-four dollars (\$1164) received for subscriptions to the *New England Journal of Medicine* from members in active service has been made over to the *Journal*, last year the comparative figure was \$750.

In 1944 total revenues to the Society amounted to \$52,903, an increase of \$935 over the previous year. Total expenses of the Society amounted to \$38,544, an increase of \$5411 over 1943. Excess of revenues over expenses was, therefore, \$14,359 for 1944.

The Society ends 1944 with total assets of cash and securities of \$272,451, an increase during the year of \$22,066.

A cordial and instructive relation has been maintained with the investment counselors. I should like to reiterate how congenial and helpful has been the aid given this office by the clerical staff of the *New England Journal of Medicine*, and to emphasize the advantage of the present close proximity of the offices for mutual speedy handling of various problems that arise.

A breakdown of comparative expenses for 1943 and 1944 is appended.

EXPENSES	1943	1944
Salaries		
Secretary	\$3000 00	\$3000 00
Executive Secretary	3000 00	3000 00
Treasurer	2000 00	2000 00
Expenses		
President	693 80	714 36
Secretary	1925 84	2195 00
Treasurer	1719 43	2113 04
Delegates to A. M. A.	689 04	779 40
Maintenance of Society Headquarters (including clerical and other expenses)	4801 56	6538 64
Shattuck Lecture	200 00	200 00
Cotting Luncheons	302 00	358 50
Committees		
Ethics and Discipline	110 71	159 07
Executive	230 21	543 47
Finance	77	16 50
Industrial Health	68 18	97 91
Information Bureau	00 00	1133 02
Legislation	297 13	204 10
Maternal Welfare	00 00	1 58
Medical Advisory to OPA	00 00	7 83
Medical Defense	707 47	1113 03
Medical Education	00 00	89
Membership	38 20	76 96
Military Postgraduate	677 60	411 06
Obstetrics and Gynecology	90 00	00 00
Postgraduate Instruction	15 19	4 60
Postwar Loan Fund	6 55	00 00
Postwar Planning	00 00	116 01
Postpayment Medical Care	00 00	44 50
Prepaid Medical Care	00 00	24 28
Public Health	10 00	164 06
Public Relations	182 39	56 03
Wagner Bill Conference	00 00	209 61
War Participation	234 78	
Publications		
<i>New England Journal of Medicine</i>	7000 00	7900 00
<i>Directory</i>	187 31	51 36
Refunds to district societies	4000 00	4000 00
Refunds to fellows on active service	176 00	28 00
<i>N. E. J. of M.</i> for subscriptions to <i>Journal</i> from fellows in active service	750 40	1164 00
Net loss on securities sold called or matured	18 46	00 00
	\$33 133 02	\$38 544 33

ELIOT HUBBARD, JR., Treasurer

APPENDIX NO 2

REPORT OF THE COMMITTEE ON MEMBERSHIP

The Committee on Membership, meeting with the supervising censors, as provided in Chapter V, Section 1, of the by-laws, recommends

That the following-named fellows applying for retirement and with all dues paid and in good standing, be allowed to retire under the provisions of the by-laws, Chapter I, Section 5

Balch, Franklin G (Norfolk), 109 Moss Hill Road, Jamaica Plain

Dewis, John W (Essex South), 7 Gregory Street, Marblehead (Journal requested)

Dunn, William A (Suffolk), 39 Somerset Street, Boston.

Harriman, Perley (Essex South), 11 Atlantic Street, Lynn (Journal requested)

Howell, William W (Norfolk), 44 Eliot Street, Jamaica Plain

Leland, Forrest L (Hampden), 6 Gaylord Street, South Hadley Falls

MacCorison, Carl C (nonresident), North Berwick, Maine.

MacLennan, Angus D (Suffolk), 411 Marlboro Street, Boston

Moore, Fredrika (Middlesex South), 983 Memorial Drive, Cambridge

Newhall, Harvey F (Essex South), 51 Nahant Street, Lynn

Royal, Herbert B (Worcester), Still River Road, Harvard (Journal requested)

Smith, Hervey L (Hampden), 235 Queens Lane, Palm Beach, Florida

Sullivan, Cornelius A (Norfolk South), 20 Pond Street, South Braintree (Journal requested)

Sullivan, Joseph L (Norfolk), 89 Waverley Street, Roxbury

That the following-named fellows applying for resignation and with all dues paid and in good standing, be allowed to resign under the provisions of the by-laws, Chapter I, Section 7, such resignation effective January 1, 1945

Kirkpatrick, Milton E (nonresident), 1737 Prytania Street, New Orleans, Louisiana

McKhann, Charles F (nonresident), P O Box 118, R P Annex, Detroit 32, Michigan

That the following-named fellow applying for resignation be allowed to resign, with remission of dues owed the Society, under the provisions of the by-laws, Chapter I, Sections 6 and 7 of the by-laws, such resignation effective January 1, 1945

Clarke, Samuel T (nonresident), 240 West First Street, Reno, Nevada

That the following-named fellows, who are ill and incapacitated, shall have the dues owed the Society remitted under the provisions of the by-laws, Chapter I, Section 6

Harkins, William J (Norfolk South), 20 Whitney Street, Quincy 1945

Krieger, William L (Norfolk South), 15 Lincoln Avenue, Wollaston 1945

Shukle, R M (Suffolk), 432 Marlboro Street, Boston 1944 and 1945

That the following-named fellow, who had resigned from the Society while in good standing, be reinstated under the provisions of the by-laws, Chapter I, Section 10

Wilens, Gustav (Middlesex South), Cochituate Road, Wayland

That the following-named fellows, who have been deprived of membership for the nonpayment of dues, be reinstated as fellows of the Society, provided their arrears in dues at the time of deprivation, plus their dues for the year 1945 be sent to the treasurer of the Society, in accordance with the by-laws, Chapter I, Section 10

Aschillo, H V (Hampshire), 16 Centre Street, Northampton

Butler, Harry H (Norfolk), 48 Winchester Street, Brookline

Rosen, Edward (Suffolk), 164 Shirley Avenue, Revere

That the following-named fellows be allowed to change their membership from one district society to another, with out change of legal residence, under the provisions of the by-laws, Chapter III, Section 3

Anderson, Donald G, 46 Orchard Street, Jamaica Plain (Remain in Suffolk)

Anderson, Erna G, 46 Orchard Street, Jamaica Plain (Remain in Suffolk)

Goodman, Joseph, Clay Brook Road, Dover (Remain in Middlesex South)

Hvde, Harold V, 987 Memorial Drive, Cambridge
(Remain in Suffolk)
Joice, Charles C, 31 Conant Street, Danvers
(Essex South to Plymouth)
McMackin, Francis L, 230 Brattle Street, Cambridge
(Norfolk to Suffolk.)
Robins, Samuel A, 15 Galvin Road, Newton Centre
(Middlesex South to Norfolk.)
Todd, John J, 23 Windmere Road, Milton
(Remain in Suffolk.)

Committee on Membership

HARLAN F NEWTON, *Chairman*
JOHN E FISH
PEIRCE H LEAVITT
SAMUEL N VOSE
ROY V BAKETEL

Supervising Censor

WILLIAM H ALLEN
H QUIMBY GALLUPE
ALBERT E PARKHURST

APPENDIX NO 3

REPORT OF THE COMMITTEE ON PUBLIC RELATIONS

There have been two meetings of the Committee on Public Relations. A summary of the report of the first meeting has been sent you.

The second meeting was held on April 25, 1945, and unfortunately your secretary was unable to be there. There were present, in addition to President Bagnall and Secretary Tighe, representatives from nine districts. The first subject studied was a report of the Subcommittee on Public Information, which was received and approved. This report is to be given by the chairman of the Subcommittee, Dr John Fallon. The second question studied was a report of the Subcommittee on Tax-Supported Medical Care, which will be given later by Dr Dumphy. This report was discussed at some length and approved with two members dissenting.

The summary of the report of the first meeting is as follows:

The members of this committee listened with great interest to a recital of the activities of the Committee on Postwar Planning by Dr Howard F Root, its chairman. It expressed a desire to support these activities in every way possible.

The Subcommittee on Labor and Industry presented an interesting report on its activities to date. It was the belief of the Committee on Public Relations that the subcommittee should pursue its activities. A report of progress will be presented by this subcommittee later in this meeting.

The Subcommittee on Tax-Supported Medical Care reported on certain conversations that it had in March with Mr Long, Commissioner of Veterans Aid and Pensions, anent payments for the medical treatment of needy veterans. This subcommittee signified that it intended to consult with the Massachusetts Commissioner of Welfare along the same lines. The Committee on Public Relations approves the report and the recommendations contained therein. The Committee on Public Relations recommended that the Subcommittee on Tax-Supported Medical Care reconsider the question of charges to recipients of welfare assistance and old-age assistance with a view that payment be made for all medical and surgical services rendered.

After considerable discussion with Dr Vlado A Getting, Commissioner of Public Health, and Dr Geoffrey Edsall, of that department, the Committee on Public Relations approved, in principle, the plan of the Department of Public Health for the collection of blood, voluntarily donated, and the distribution of the fractions of the blood to the citizens of Massachusetts without charge. Such distribution is to be made on the recommendation of physicians.

ALBERT A HORNOR, *Secretary*

APPENDIX NO 4

REPORT OF THE COMMITTEE ON LABOR AND INDUSTRY

The Subcommittee on Labor and Industry of the Committee on Public Relations offers this report as one of information only.

The subcommittee had separate conferences with representatives of the two major labor groups in Massachusetts — the CIO and the A F of L. These conferences were held for the purpose of obtaining first-hand knowledge of the feeling of labor with regard to medical care and how it is to be paid for.

It was found that both these groups have definite ideas as to their demands in this matter. The CIO defines these demands in terms of the following language: "Adequate medical care at the price the worker is able to pay." The A F of L says its demands can be met by an insurance scheme, the entire cost of which is to be borne by industry. The subcommittee has reason to believe that this very same view is held by the CIO although this fact did not come out in our conference with its representatives.

The representatives of both organizations disclaimed any desire to see the Government in this field, provided their demands could be met in any other way, because in a government scheme labor would undoubtedly be compelled to contribute its share of the costs.

The subcommittee learned that, in lieu of wage increases which could not be granted because of the Little Steel Formula, many industries had contracted with private insurance carriers to cover the medical-care costs or part of these costs incurred by their employees when ill.

The subcommittee also learned that the Massachusetts office of the National Labor Relations Board frequently took a hand in the negotiations leading to this end. This latter information has been passed on to the Blue Shield and Blue Cross as suitable fields to explore. We are informed that these conferences have already resulted in an increased enrollment by CIO members in the Blue Shield.

The subcommittee finds from another source how widespread has become the practice of providing for the medical-care costs of those employed in industry through private carriers. Reference here is to the report of the Advisory Council of the Massachusetts Unemployment Commission which says that, of the 780,000 people in Massachusetts employed in industry, over 60 per cent have, through private carriers, provided for their medical-care costs in whole or in part.

Supplementing the meetings that the committee had with representatives of the CIO and the A F of L, a meeting was held with a committee of the Associated Industries of Massachusetts on May 9, 1945, at the Hotel Kenmore. Those present were Mr Lawrence Muench, president of Hood Rubber Company, Watertown, Mr Philip M Morgan, president of the Morgan Construction Company, Worcester, Mr Horace C Houghton, personnel director of the Bethlehem Quincy Yard and assistant to the general manager, Mr George E Williamson, vice-president and treasurer of the Strathmore Paper Company, Springfield, Mr Roy F Williams, executive vice-president of the Associated Industries, and Mr Jarvis Hunt, attorney for the Associated Industries.

The general subject of medical-care costs was informally discussed, a subject in which these representatives of industry were vitally interested. In their opinion there were two phases of this problem — one relating to medical care and its costs and the other to the income of the employee during his illness. After considerable discussion it was their opinion that the cost of medical care could not be borne by industry at the present time. The reason given for this opinion was that, if borne by industry, it would be an additional cost to production thereby rendering their cost higher than that of their competitors in neighboring states, who did not have the same coverage. They felt that the payment of benefits to employees was a social and economic problem and should probably be covered by state or national legislation. Each of these representatives of industry cited systems in practice at their places of business with reference to accident insurance. In all cases, the cost of this insurance was paid for by the employee by weekly deductions from his salary, but the operating expenses, such as rooms, clerical help and investment of funds, were borne by the employer. A general dis-

cussion was entered into with reference to the Vaughn Bill now before the Legislature, which contains liberal accident and health benefits and would presumably be administered by a board, such as the Industrial Accident Board. It was generally agreed by those present that such legislation was a step toward state medicine, which, in the end, might lead to national medical supervision. Therefore, at the present time, they were not in favor of such legislation. It was an interesting two-hour discussion.

DANIEL B. REARDON, *Chairman*
 GEORGE J. CONNOR
 DANIEL J. ELLISON
 JOHN FALLON
 MICHAEL A. TIGHE

APPENDIX NO 5

PROPOSED RULES OF THE MASSACHUSETTS DEPARTMENT OF PUBLIC WELFARE FOR REIMBURSEMENT FOR PHYSICIANS' SERVICES IN HOSPITALS IN WHICH THE STAFF DOES NOT GIVE FREE CARE TO WARD PATIENTS

The department will participate in grants to recipients of public assistance for physicians' services in hospitals in which the staff does not give free care. This policy applies only to those hospitals that are approximately fifteen miles or more distant from any hospital in which free care by the staff may be obtained. A tentative list of these hospitals is as follows:

Plunkett Memorial Hospital	Adams
Farren Memorial Hospital	Montague
Franklin County Public Hospital	Greenfield
Fairview Hospital	Great Barrington
North Adams Hospital	North Adams
Wing Memorial Hospital	Palmer
Mary Lane Hospital	Ware
Community Memorial Hospital	Ayer
Webster District Hospital	Webster
Emerson Hospital	Concord
St. Luke's Hospital	Middleboro
Norwood Hospital	Norwood
Jordan Hospital	Plymouth
Cape Cod Hospital	Hyannis
Tobey Hospital	Wareham
Nantucket Cottage Hospital	Nantucket
Martha's Vineyard Hospital	Oak Bluffs

In some instances, the staff gives free care to ward patients from the community in which the hospital is located, and it is expected that this policy will continue. Exception to this list of hospitals will be made in the event of an emergency in which the nearest available hospital may be used and department participation will be granted.

Surgical Fees. These will be paid at a rate not to exceed the fees as listed by the Massachusetts Medical Service (Blue Shield) at the present time for each operation or procedure. All fees include preoperative and postoperative care. When two or more operations are performed for the same medical cause within two months, total surgical fees shall not exceed \$150.00. Care needed beyond this time will be reimbursed according to the schedule of medical fees. Fees for assistant surgeons, when necessary, will be included in the total surgical fees on a basis of approximately 10 per cent of the total fee.

Anesthesia. When there is no resident anesthetist in the hospital, fees for anesthesia will be allowed at a rate not to exceed the fees for anesthesia as listed by the Massachusetts Medical Service and only to a licensed physician other than the surgeon or assistant surgeon.

Medical Fees. Fee schedules for medical cases will be based on a minimum number of visits necessary for the patient. Participation by the department will not exceed the state's proportionate share of a \$4.00 fee for the first day and \$2.00 for each visit thereafter. Total reimbursement for physicians' fees during any one hospital stay for the first two months shall not exceed \$150.00. For a stay of more than two months, physicians' fees will be reimbursed at the rate of \$2.00 a visit, after the case has been discussed by the physician with the local board of public welfare.

APPENDIX NO 6

REPORT OF THE COMMITTEE ON LEGISLATION

This report may appear to the members of the Executive Committee unreasonably brief having in mind the many bills affecting one way or another the health of our citizens in which the members of the Society are naturally so much interested. To tabulate the various bills that have been heard, and to set forth the outcome of hearings on these bills without at least briefly discussing the subject matter of them would not greatly aid the members of the Executive Committee in their deliberation on these important matters of legislation.

Although there have been a great many bills that have been considered at the present time only a few have come out of committees, but one has been passed by the Senate and has been signed by the Governor. This is a bill that permits limited licensure not only to interns in hospitals but also interns and fellows in clinics, both incorporated and nonincorporated. As is the case in a great many of these bills, so in this one there were certain things that were good and certain things that we thought should not be approved. We stated our reasons for changes that we thought should have been made in the bill, but they were not made. This bill is now law.

After an all-day hearing before the Committee on Public Health, and after discussion in executive session by that committee, the bill giving chiropractors a separate board of registration was reported favorably. That bill is now in the hands of the Committee on Ways and Means and without doubt will come up for consideration in the House and perhaps in the Senate.

Your committee favored, with a single exception, House Bill 149, which permits children with rheumatic heart disease to receive treatment at the North Reading Sanatorium, that bill has been favorably reported and it, too, is now in the hands of the Committee on Ways and Means.

The annual vaccination bill was given leave to withdraw. There was considerable discussion on two bills having to do with changes in the Division of Occupational Hygiene. One of these bills would abolish the division, and that was given leave to withdraw in both House and Senate.

A bill requiring filing of annual returns by corporations conducting medical schools passed in the House and has been signed by the Governor.

The great majority of bills of interest to the members of the Society, however, are still under consideration and have not as yet been reported by the respective committees hearing these bills.

Four hearings were conducted by the Committee of Education having to do with osteopaths. There were originally three bills, so-called "osteopathic bills." One of these setting up a special board of examination in osteopathy was withdrawn. Briefly, one of the other two bills provided for the licensure in this state of a diplomate of the National Board of Osteopathic Examiners, and the second, in substance, provided that any graduate of any osteopathic school approved by the American Osteopathic Association would be permitted to take examination for registration by the Board of Registration in medicine. A good deal of groundwork was covered before we attempted to set forth our views in these matters. The Committee of Education at the State House rather felt that, if things were permitted to go along as they exist at the present time, within eight to ten years there would be no osteopaths practicing in the Commonwealth. Reliable sources indicate that 300,000 to 500,000 citizens in the Commonwealth want osteopathic physicians. In executive session the Committee of Education had interested parties appear before it and many phases of this problem were discussed.

A bill that has already had one hearing in the Senate, and which will be amended, may become law. That bill, in substance, would add two members to the present Approving Authority — one an osteopathic physician, and the second a lay person, both to be appointed by the Governor with the approval of the Council. It would further provide that a diplomate of the National Board of Osteopathic Examiners may present his or her certificate to the Board of Registration in Medicine, and at the discretion of the Board be permitted to practice medicine in this state, provided that such diplomate shall have graduated from an osteopathic school approved by the Approving Authority.

Seven full-day hearings before the Committee on Public Health were held for discussion of the group of bills that may be considered together as those affecting substandard schools. The purpose of these bills may be summarized without material inaccuracy as measures seeking to repeal the law as it now exists, or to change the law materially so as to permit graduates of any unapproved school the right to take the examination given by the Board of Registration in Medicine. These bills thus far have not been reported by the Committee on Public Health.

The members of the Committee on Legislation have worked untiringly in these matters entrusted to their care. The members of the committee are indeed grateful for the real help given us by some who voluntarily offered assistance, and from others from whom we asked help and received it. We are particularly grateful to the members of our profession engaged in general practice who have put themselves out to see to it that proper information aiding legislators in their deliberation on these matters was given to them. We know at the present time, however, that there are members of the Senate and the House who would have benefited in their thoughts on these various bills had they been given information to which they were and are entitled from members of the Massachusetts Medical Society. If reports that we have received are accurate, some of these legislators thus far have not been interviewed by any member of the Massachusetts Medical Society.

At this time it would seem to serve no useful purpose to comment on certain matters which will perhaps result in a most discouraging final outcome on the work which has been done thus far this year in matters of legislation. We ask the Executive Committee and the Council to hear us again in the matter of suggestions as to policies for the future. We have had almost daily assistance from our legal adviser, Mr. Charles J. Dunn, and for this we are indeed grateful.

This report is respectfully submitted, as heretofore stated, as a preliminary report, and on this report we ask your approval.

W E BROWNE, *Chairman*

APPENDIX NO 7

REPORT OF THE COMMITTEE ON POSTWAR PLANNING

The provision of necessary educational opportunities as well as opportunities for various types of professional activity desired by returning medical veterans is a first consideration in any plan for the postwar era. The most recent analysis of 21,000 questionnaires returned by physicians in the armed forces indicates that more than 12,000 hospital residencies or long courses of postgraduate training will be required during the two-year period of demobilization. It is possible that this figure may be too conservative, since no expression of the desires of a large percentage of doctors in the service has been obtained. Present facilities appear to provide for only half this number. Therefore, a large number of such special opportunities must be provided either by increasing the appointments in existing hospitals or by adding new hospitals. Hospitals not now provided with interns and residencies need to organize teaching services for the training of such men.

The returns from this questionnaire indicate how fully the recent graduate in medicine appreciates the inadequacy of his training particularly along clinical lines. It is not sufficient to dismiss this as one of the exigencies of the war. If the same high standards of medical care to which the American people have been accustomed is to be maintained, notice must be taken of the inadequacy in preparation which looms large in the doctor trained in wartime and every effort bent toward its relief. The committee believes that the hospitals of the Commonwealth can and should play a most important part in any program directed toward that end.

Economic aspects of postwar practice are emphasized (*JAMA*) 128 (38-41, 1945) by a further analysis of these questionnaires which shows a large percentage of the medical officers in the group studied are interested in future specialty practice. Indeed, the group represented about half again as many as originally were engaged in special fields. In answer to questions concerning voluntary redistribution to areas needing physicians the important point came

out that nearly 29 per cent, or 6091, would go to such areas if there were hospital facilities. About 85 per cent of the officers indicated they did not desire to remain in government service.

One fifth of all medical officers who returned the questionnaire indicated an interest in the field of industrial medicine. Four times as many men wanted part-time positions in industrial medicine as wanted full-time positions. An important point is that many of those who wish to engage in part-time industrial practice would also like to take special training. It is clear that soon many questions will be addressed to us by medical officers in anticipation of their discharge from the Army within six months or a year seeking information about possible residencies, special courses from three to six months or longer in special cases but also opportunity for part-time or full-time work in industrial medicine or even full-time salary position in state hospitals as well as opportunities for location in private practice.

Provision should be made therefore to set up a service bureau at the society headquarters that can give information by mail or in person regarding the wide variety of opportunities in this state. This service bureau might naturally include the present Bureau of Clinical Information and it would necessarily work in close co-operation with the medical schools, which would be glad to refer men to it for information. This bureau would also work closely with the central bureau of the American Medical Association at Chicago. The Bureau of Information of the American Medical Association has set about collecting and tabulating information on medical facilities and needs for some months. This bureau has sent summary sheets to every county by states in the United States. These summary sheets will provide information about the population, number of physicians in each county, the economic status of that county as indicated by the size of its cities, the retail purchases per year and so forth. When these sheets have been analyzed the data will be available to each state and county unit for use in such local service bureaus as proposed here. Already more than half the Massachusetts district societies have sent in their summary sheets. It appears likely that as the months pass and the end of the war approaches the need for extra personnel at such a bureau at 8 Fenway may become urgent.

This bureau, then, under a central co-ordinating committee might serve not merely during the postwar period but afterward as an integrating agency for postgraduate instruction of all kinds in hospitals, medical schools and elsewhere for the service not only of returning veterans but also of all doctors and medical agencies.

The establishment of a permanent veterans' medical and hospital service in the Veterans Administration is proposed in a bill in the House of Representatives by Mrs. Rogers of Massachusetts and in a second bill by Mr. Priest of Tennessee. These two bills will be the subject of a report by a special committee of the Committee on Postwar Medical Service.

The physical fitness program will become increasingly important in the future, and leadership by the medical profession should not be withheld. The placing of four million Americans in Class 4F by Selective Service is the reason for anticipating a program for future aims at early correction and prevention of disqualifying defects.

Mr. Joseph Lawrence, director of the Washington office of the Council on Medical Service and Public Relations of the American Medical Association, recommends to all interested physicians the two pamphlets (Parts 5 and 6) covering the hearings of the Pepper Committee, officially entitled "The Subcommittee of the Committee on Education and Labor, United States Senate, Wartime Health and Education."

Postgraduate education must be provided in medical schools and in hospitals, but also in communities at a considerable distance from medical schools. Education must become a prime function of the medical society and of the hospital, and its importance to the medical care of the American people must be understood in the future by trustees, laymen, editors, representatives of labor and allied organizations. Thus, a major objective must be the securing of better co-operative teamwork between physicians, dentists, nurses and public-health agencies, both public and private.

Modern medical methods of diagnosis and therapeutics require more skill, more education, more time, more equipment and more intelligent co-operation by patient and doctor than ever before. To attain a better quality with wider

distribution of medical care and lower costs must be an objective of us all. Prepayment sickness insurance plans need further study and trial.

It was obvious to the committee that its work must be carried out through subcommittees. Reports so far received from subcommittees may be briefly summarized.

Subcommittee on Hospitals, Dr Nathaniel Faxon, chairman. Although there are more than 200 hospitals in Massachusetts, of which 125 belong to the American Hospital Association, a recent analysis showed that only 35 hospitals were approved for offering residencies. More hospitals in Massachusetts and New England should organize staff members for teaching interns and residents. It is not essential that the hospital be large. Doctors genuinely interested in teaching can convey to an intern excellent teaching in a 35-bed hospital. Yet larger hospitals afford a more varied experience. Already first steps have been taken in the preparation of a statement intended for use by hospitals that desire to organize their staffs and resident services in order that they may classify as teaching hospitals. The details of this program, easily understood by physicians, are not so clear or so necessary in the minds of lay people. Joint meetings of staff and lay people in each community for improving and extending the educational service of hospitals not only to the interns but to the hospital staff and to patients as well are needed.

The Advisory Committee appointed by Governor Tobin will conduct a survey both of Massachusetts hospitals and nursing homes, which should provide entirely new data regarding medical care and medical needs in the Commonwealth.

Subcommittee on Medical Schools, Dr Charles F Branch, chairman. The medical schools of today are keenly interested in extending their service to the community. Their faculties possess special knowledge in the basic sciences which can be brought to medical groups at a distance by better organization of teaching through the Society's efforts.

Subcommittee on Postgraduate Education, Dr Richard Ohler, chairman. In an era of rapid scientific discovery varied and continuous programs of postgraduate instruction are necessary. No doctor five years out of medical school or more can practice successfully with the education acquired in his undergraduate years. Effort is being made to develop a varied program making use of hospitals and centers of education remote from metropolitan areas as well as in university centers and utilizing the co-operation of the Department of Public Health and Department of Education. The committee plans a limited number of teaching centers, each to act as a focus for a district circuit. The program should begin in the fall of 1945, and a detailed report will follow later.

Our present aim is to bring about a better understanding among physicians, hospital trustees and public-health agencies of the present unique opportunities presented to American medicine. Never before has the interest of the lay public in hospitals, doctors and medicine been so great. It has been stimulated by the war, and particularly by active participation as volunteers in hospitals and public-health organizations of men and women never before in immediate contact with such work. The public interest has been most clearly presented in the report presented before Senator Pepper's Subcommittee on Wartime Health and Education, whose hearings began last July and are still in progress. A series of meetings should be carried out in hospitals throughout the Commonwealth where physicians of hospital staffs, together with hospital trustees, editors and representatives of labor, may discuss under a panel form of program various proposals for providing hospital internships and residencies and extending medical care in the immediate community as well as in the Commonwealth. Speakers may be secured through this committee.

It is recommended that committees on postwar plans in each district society study the possibility of increasing the hospital residencies to be available for veteran physicians.

A meeting will be held Wednesday, June 20, at 5:00 p.m., at the Hotel Puritan of representatives of hospitals who wish to discuss plans for new internships and residencies. The provisions of the G. I. Bill of Rights become applicable to hospitals or other institutions offering educational opportunities when their residencies or other courses have been approved by the Board of Collegiate Authority, 200 Newbury Street, Boston. Hospitals are invited to be repre-

sented by the superintendent, trustees and a member of the medical attending staff.

HOWARD F. ROOT, Chairman
LEROY E. PARKINS, Secretary

APPENDIX NO 8

REPORT OF THE COMMITTEE ON ETHICS AND DISCIPLINE

The Committee on Ethics and Discipline is happy to report to the Executive Committee of the Council of the Massachusetts Medical Society that the ethical health of the Society is excellent. Only twenty complaints have been received to date for the year 1944-1945. However, each of these complaints, no matter how trivial, required investigation, hearings and discussion. The majority of the complaints were from laymen accusing fellows of unethical practice.

Two of these complaints were brought as a prelude to court procedure — the cases already slated for trial. These the committee refused to consider until judicial decision had been handed down.

The remaining cases of this group were thoroughly investigated, hearings given to both complainant and the accused fellow. In each case there was found to be either animosity or hope of financial gain on the part of the complainant, and the fellow was an innocent sufferer.

Two cases were referred to the committee from the State Board of Registration in Medicine concerning alleged unethical action on the part of two fellows — one of improper testimony in a trial, the other of falsifying records. The first fellow, after investigation, was judged to be innocent of unethical deportment, although his lack of judgment was evident. The second fellow was found guilty of falsifying his records and of giving false testimony on interrogation as to his actions. He was referred to the President for severe admonition.

Two cases concerned accusation of violation of the Code of Ethics by fellow against fellow.

The first case was dismissed because of the lack of real evidence of wrongdoing. In the second case, the defendant was found guilty of unethical conduct in advising with and the treatment of a patient still under the care of the complainant. The offending fellow was requested by the committee to send a written apology to the injured fellow. This was sent, accepted, a copy sent to the committee and the incident declared closed.

On April 11, 1945, the committee dealt with a case in which a fellow of the Society was charged with a serious violation of the Code of Ethics. He was found guilty and severely reprimanded by the President at the request of the committee.

WILLIAM J. BRICKLEY
ALLEN G. RICE
FRED R. JOUETT
ARCHIBALD R. GARDNER
RALPH R. STRATTON, Chairman

APPENDIX NO 9

PROPOSAL BY THE RHODE ISLAND MEDICAL SOCIETY FOR A COUNCIL OF THE MEDICAL SOCIETIES OF NEW ENGLAND

PREAMBLE

The main purpose of such a council would be to bring about closer co-operation between the medical societies of the New England states in the development of plans relative to organized medicine, and plans for the furtherance of all phases of public health under medical supervision.

Recognizing that each society has problems peculiarly its own that cannot be solved by any general provision, the council might serve as a body to deliberate on those larger matters in which each of the societies is equally concerned. Also, in view of the fact that each society is a component unit of the American Medical Association, this council should

now the principle that it shall not seek to supersede the control now exercised on organized medicine by the House of Delegates of the national organization

ORGANIZATION

The council might be composed of the presidents or secretaries of the constituent state societies, and of two additional representatives, who shall be appointed by the president or the governing body of the respective state society as it may determine, each to serve for stated terms

Officers of the council might be elected by the council itself, to serve for one year, or until their successors were duly qualified and elected

Meetings might be held at stated times during the year, and alternately in the various states, and also might be held at such other times as deemed necessary by the president of the council

The council might make such rules and regulations as it deemed advisable and necessary for its successful operation

The expenses of the council organization might be prorated annually among the six state medical societies

METHOD OF PROCEDURE

The council might consider any problem submitted by a member society, or its representative, that might in any manner affect organized medicine or public health in New England, or in any part of New England. A majority vote might be deemed sufficient to pass any measure, but all council legislation might be submitted to the governing body of each constituent society for action. If one or more of these bodies rejected any measure in a stated time from the date the report of the measure is made by the secretary of the council, the measure then might be reconsidered at the next meeting of the council. If, at such subsequent meeting the measure was passed by a two-thirds vote of the council, it would then become a council act

The council might also serve well as a body, to initiate studies on problems of mutual interest to the member societies—for example, plans and programs for voluntary medical care, group hospitalization, participation in federal-state programs, postgraduate medical education, public relations relative to the problems of organized medicine, national and local health legislation, development of the medical publications within the various states and the assignment of meeting dates to eliminate conflicts in securing guest speakers and in procuring technical exhibits

OFFICERS FOR 1945-1946

- PRESIDENT Reginald Fitz, Brookline Office, Boston (15), 319 Longwood Avenue
 PRESIDENT-ELECT Dwight O'Hara, Waltham Office, Boston (15), 416 Huntington Avenue
 VICE-PRESIDENT William Jason Mixer, Brookline Office, Boston (15), 319 Longwood Avenue
 SECRETARY Michael A Tighe, Lowell Office, Boston (15), 8 Fenway
 TREASURER Eliot Hubbard, Jr, Cambridge, 29 Highland Street
 ASSISTANT TREASURER Norman A Welch, West Roxbury Office, Boston (15), 520 Commonwealth Avenue
 ORATOR Frank H Lahay, Boston (15), 605 Commonwealth Avenue

COMMITTEES ELECTED BY THE DISTRICTS

- EXECUTIVE COMMITTEE OF THE COUNCIL—Established 1941 (Members *ex-officio* and one councilor and alternate elected by the councilors of each district medical society)
 PRESIDENT Reginald Fitz, Brookline Office, Boston (15), 319 Longwood Avenue
 PRESIDENT-ELECT Dwight O'Hara, Waltham Office, Boston (15), 416 Huntington Avenue
 VICE-PRESIDENT William Jason Mixer, Brookline Office, Boston (15), 319 Longwood Avenue
 SECRETARY Michael A Tighe, Lowell Office, Boston (15), 8 Fenway
 TREASURER Eliot Hubbard, Jr, Cambridge, 29 Highland Street

Term Expires 1946

- BARNSTABLE Paul M Butterfield, Harwich (Alternate William D Kinney, Osterville)

- BRISTOL NORTH William H Allen, Mansfield, 70 North Main Street (Alternate Ralph M Chambers, Taunton, Taunton State Hospital)
 BRISTOL SOUTH Edwin D Gardner, New Bedford, 150 Cottage Street (Alternate George W Blood, Fall River, 82 New Boston Road)
 ESSEX NORTH Frank W Snow, Newburyport, 24 Essex Street (Alternate Rolf C Norris, Methuen, 247 Broadway)
 MIDDLESEX EAST Edward M Halligan, Reading, 37 Salem Street (Alternate Richard Dutton, Wakefield, 33 Avon Street.)
 PLYMOUTH Peirce H Leavitt, Brockton, 129 West Elm Street (Alternate)

Term Expires 1947

- BERKSHIRE Isaac S F Dodd, Pittsfield, 34 Fenn Street (Alternate Patrick J Sullivan, Dalton 471 Main Street)
 FRANKLIN William J Pelletier, Turners Falls 113 Avenue A (Alternate John E Moran, Greenfield, 31 Federal Street)
 HAMPDEN William A R Chapin, Springfield, 121 Chestnut Street. (Alternate Edward P Bagg, Holyoke, 207 Elm Street)
 MIDDLESEX NORTH William F. Ryan, Lowell, 219 Central Street (Alternate William M Collins, Lowell, 174 Central Street)
 NORFOLK Charles J Kickham, Brookline Office, Boston (15), 524 Commonwealth Avenue (Alternate Henry M Emmons, Boston, 354 Commonwealth Avenue)
 WORCESTER NORTH C Bertram Gay, Fitchburg 62 Day Street (Alternate George P Keaveny, Fitchburg, 62 Fox Street)

Term Expires 1948

- ESSEX SOUTH Walter G Phippen, Salem, 31 Chestnut Street (Alternate Bernard Appel, Lynn, 281 Ocean Street)
 HAMPSHIRE Joseph D Collins, Northampton, 187 Main Street (Alternate William M Dobson, Northampton, Veterans Administration Facility)
 MIDDLESEX SOUTH Harold G Giddings, Newton Centre Office, Boston (16), 270 Commonwealth Avenue (Alternate Arthur M Jackson, Everett (49), 512 Broadway)
 NORFOLK SOUTH Daniel B Reardon, Quincy (69), 1186 Hancock Street (Alternate Nahum R Pillsbury, South Braintree (85) Norfolk County Hospital)
 SUFFOLK Alexander J A Campbell, Boston (15), 520 Commonwealth Avenue (Alternate Howard F Root, Boston (15), 81 Bay State Road)
 WORCESTER Bancroft C Wheeler, Worcester, 27 Elm Street (Alternate John J Dumphy, Worcester, 390 Main Street)

COMMITTEE ON PUBLIC RELATIONS—Established 1931 (One councilor elected yearly by each district medical society, the president and president-elect of the Society are chairman and vice-chairman, respectively, and the vice-president and secretary of the Society are members *ex officio*)

- BARNSTABLE William D Kinney, Osterville
 BERKSHIRE Patrick J Sullivan, Dalton, 471 Main Street.
 BRISTOL NORTH James H Brewster, Attleboro, 178 South Main Street
 BRISTOL SOUTH
 ESSEX NORTH Harold R Kurth, Lawrence, 57 Jackson Street
 ESSEX SOUTH Loring Grimes, Swampscott, 84 Humphrey Street
 FRANKLIN John E Moran, Greenfield, 31 Federal Street
 HAMPDEN Patrick E Gear, Holyoke, 188 Chestnut Street
 HAMPSHIRE William M Dobson, Northampton, Veterans Administration Facility
 MIDDLESEX EAST Milton J Quinn, Winchester, 44 Church Street.
 MIDDLESEX NORTH Daniel J Ellison, Lowell, 8 Merrimack Street
 MIDDLESEX SOUTH Gordon M Morrison, Waban Office, Boston (15), 520 Commonwealth Avenue
 NORFOLK Norman A Welch, West Roxbury Office, Boston (15), 520 Commonwealth Avenue
 NORFOLK SOUTH Nahum R Pillsbury, South Braintree (85), Norfolk County Hospital
 PLYMOUTH Charles D McCann, Brockton 12 Cottage Street.

SUFFOLK Albert A Hornor, Boston (15), 319 Longwood Avenue
 WORCESTER John Fallon, Worcester, 390 Main Street
 WORCESTER NORTH James V McHugh, Leominster, 100 Main Street
 COMMITTEE ON LEGISLATION — Established 1942 (One councilor elected yearly by each district medical society)
 BARNSTABLE Julius G Kelley, Pocasset, Barnstable County Sanatorium
 BERKSHIRE Clement F Kernan, Pittsfield, 184 North Street
 BRISTOL NORTH Ralph M Chambers, Taunton, Taunton State Hospital
 BRISTOL SOUTH
 ESSEX NORTH Edward H Ganley, Methuen, 251 Broadway
 ESSEX SOUTH Charles A Worthen, Lynn, 19 Park Street
 FRANKLIN Howard M Kemp, Greenfield, 42 Franklin Street
 HAMPDEN Arthur H Riordan, Indian Orchard, 147 Oak Street
 HAMPSHIRE Arthur N Ball Northampton, State Hospital
 MIDDLESEX EAST John M Wilcox, Woburn, 6 Bennett Street
 MIDDLESEX NORTH Archibald R Gardner, Lowell, 16 Shattuck Street.
 MIDDLESEX SOUTH Edward J O'Brien, Brighton Office, Boston (16), 270 Commonwealth Avenue
 NORFOLK Humphrey L McCarthy, West Roxbury Office, Boston (15), 479 Beacon Street
 NORFOLK SOUTH David L Belding, Hingham Office, Boston (18), 80 East Concord Street
 PLYMOUTH John J McNamara, Brockton, 231 Main Street.
 SUFFOLK William E Browne, Boston (15), 587 Beacon Street. (Chairman)
 WORCESTER Lester M Felton, Worcester, 36 Pleasant Street
 WORCESTER NORTH Donald B Cheetham, Athol, 164 Exchange Street
 COMMITTEE ON NOMINATIONS Established 1874 (One councilor and alternate elected yearly by each district medical society)
 BARNSTABLE William D Kinney, Osterville (Alternate Paul M Butterfield, Harwich)
 BERKSHIRE Patrick J Sullivan, Dalton, 471 Main Street (Alternate Charles F Fasce, Pittsfield, 311 North Street.)
 BRISTOL NORTH William H Allen, Mansfield, 70 North Main Street (Alternate Joseph L Murphy, Taunton, 23 Cedar Street)
 BRISTOL SOUTH Edmond F Cody, New Bedford, 105 South 6th Street (Alternate Richard B Butler, Fall River, 278 North Main Street)
 ESSEX NORTH Guy L Richardson, Haverhill, 94 Emerson Street (Alternate Rolf C Norris, Methuen, 247 Broadway)
 ESSEX SOUTH Paul E Tivnan, Salem, 70 Washington Street (Alternate Peer P Johnson, Beverly, 1 Monument Square)
 FRANKLIN William J Pelletier, Turners Falls, 113 Avenue A (Alternate Howard M Kemp, Greenfield, 42 Franklin Street)
 HAMPDEN Allen G Rice, Springfield, 146 Chestnut Street (Alternate Harry F Byrnes, Springfield, 6 Chestnut Street)
 HAMPSHIRE Henry A Tadgell, Belchertown, Belchertown State School (Alternate Joseph D Collins, Northampton, 187 Main Street)
 MIDDLESEX EAST Ralph R Stratton, Melrose (76), 538 Lynn Fells Parkway (Alternate Edward M Halligan, Reading, 37 Salem Street)
 MIDDLESEX NORTH James J Cassidy, Lowell, 9 Central Street (Alternate William M Collins, Lowell, 174 Central Street)
 MIDDLESEX SOUTH Dwight O'Hara, Waltham Office, Boston (15), 416 Huntington Avenue (Alternate Joseph C Merriam, Framingham, 198 Union Avenue)
 NORFOLK Albert Ehrenfried, Brookline Office, Boston (15), 520 Commonwealth Avenue (Alternate Carlton E Allard, Dorchester, 428 Columbia Road)
 NORFOLK SOUTH Daniel B Reardon, Quincy (69), 1186 Hancock Street (Alternate James E Knowlton, Wollaston (70), 579 Hancock Street)
 PLYMOUTH Bradford H Peirce, South Hanson, Plymouth County Hospital (Alternate George A Moore, Brockton, 167 Newbury Street)

SUFFOLK Albert A Hornor, Boston (15), 319 Longwood Avenue (Alternate Conrad Wesselhoeft, Boston, 11 Marlboro Street.)
 WORCESTER William F Lynch, Worcester, 390 Main Street (Alternate Ralph S Perkins, Worcester, 10 Hackfield Road)
 WORCESTER NORTH James V McHugh, Leominster 100 Main Street (Alternate George P Keaveny, Fitchburg, 62 Day Street)

STANDING COMMITTEES FOR 1945-1946

(ELECTED BY THE EXECUTIVE COMMITTEE OF THE COUNCIL, MAY 23, 1945)

ARRANGEMENTS — Established 1849

	<i>Date of Appointment</i>
Roy J Heffernan, Norfolk, Chairman	May 25, 1942 (appointed chairman May 22, 1944)
G Guy Bailey, Jr, * Middlesex South	November 13, 1942
Harold G Giddings, Middlesex South	May 22, 1944
Robert L Goodale, Suffolk	May 22, 1944
Sidney C Wiggan, Suffolk	June 24, 1942

ETHICS AND DISCIPLINE — Established 1871

Ralph R Stratton, Middlesex East, Chairman	June 9, 1936 (appointed chairman May 21, 1941)
William J Brickley, Suffolk	February 3, 1937
Archibald R Gardner, Middlesex North	May 21, 1941
Fred R Jouett, Middlesex South	May 21, 1940
Allen G Rice, Hampden	June 1, 1938

FINANCE — Established 1938

Francis C Hall, Suffolk, Chairman	July 8, 1943
Ernest L Hunt, Worcester	June 2, 1938
Edward J O'Brien, Jr, Middlesex South	June 2, 1938
Peer P Johnson, Essex South	October 4, 1939
Charles F Wilinsky, Suffolk	June 2, 1938

INDUSTRIAL HEALTH — Established 1942

Thomas L Shipman, Essex South, Chairman	May 25, 1942 (appointed chairman [interim appointment] June 29, 1945)
Joseph C Aub, Suffolk	May 25, 1942
Louis R Daniels, Middlesex South	May 22, 1944
John G Downing, Middlesex South	May 22, 1944
Patrick E Gear, Hampden	May 23, 1945
Harold R Kurth, Essex North	May 23, 1945
Daniel L Lynch, Norfolk	May 25, 1942

MEDICAL DEFENSE — Established 1927

Arthur W Allen, Suffolk, Chairman	June 7, 1927 (appointed chairman June 7, 1939)
Ira M Dixon, Berkshire	August 17, 1942
Edwin D Gardner, Bristol South	June 7, 1927
William R Morrison, Suffolk	June 9, 1936
Horatio Rogers, Suffolk	June 7, 1939

MEDICAL EDUCATION — Established 1881

Robert T Monroe, Norfolk, Chairman	May 21, 1941 (appointed chairman February 4, 1942)
Arthur W Allen, Suffolk	May 24, 1943
George D Henderson, Hampden	June 1, 1938
Isaac R Jankelson, Norfolk	May 25, 1942
Chester S Keefer, Suffolk	February 4, 1942

*Italics indicate that the physician is not a member of the Council of the Society

MEMBERSHIP — Established 1897

- Harlan F Newton, Suffolk,
Chairman
June 9, 1931 (ap-
pointed chairman
May 25, 1942)
Roy V Baketel, Essex North
January 10, 1945
William A R Chapin, Hampden
May 23, 1945
Perce H Leavitt, Plymouth
June 1, 1938
Samuel N Vose, Suffolk
March 15, 1944
William H. Allen (Bristol North), H Quimby Gallupe (Mid-
dlesex South), Albert E Parkhurst (Essex South), represent-
ing the Supervising Censors

PUBLICATIONS — Established 1825

- Richard M. Smith, Suffolk,
Chairman
June 6, 1933 (ap-
pointed chairman
May 21, 1941)
Oliver Cope, Middlesex South
May 21, 1941
John Fallon, Worcester
November 14, 1944
James P O'Hare, Suffolk
June 9, 1936
Conrad Wesselhoeft, Suffolk
June 2, 1937

PUBLIC HEALTH — Established 1912

- Roy J Ward, Worcester, Chairman
May 22, 1944
Elmer S Bagnall, Essex North
May 23, 1945
Ernest M Morris, Middlesex South
May 22, 1944
George L Steele, Hampden
May 23, 1945
Conrad Wesselhoeft, Suffolk
July 27, 1944

SOCIETY HEADQUARTERS — Established 1942

- Frank R Ober, Suffolk,
Chairman
May 22, 1944 (ap-
pointed chairman
November 1, 1944)
Albert A Hornor, Suffolk
November 6, 1944
Charles G Mixer, Suffolk
June 8, 1942
Daniel B Reardon, Norfolk South
May 22, 1944
Michael A. Tighe, Middlesex North
May 24, 1943

ADVISORY COMMITTEE TO COMMITTEE ON INDUSTRIAL
HEALTH — Established 1942

- Manfred Bowditch, Philip Drinker, Alton Pope

SPECIAL COMMITTEES FOR 1945-1946

(ELECTED BY THE EXECUTIVE COMMITTEE OF THE COUNCIL
ON MAY 23, 1945)

COMMITTEE ON CANCER — Established 1917

- George A Moore, Plymouth, Chairman, Thomas J
Anglem, Suffolk, Ernest M Daland, Suffolk, Allen
G Rice, Hampden, Channing C Simmons, Suffolk

COMMITTEE ON COUNCIL RULES — Established 1944

- Charles E. Mongan, Middlesex South, Chairman, Elmer
S Bagnall, Essex North, Frank R Ober, Suffolk,
George Leonard Schadt, Hampden, Michael A
Tighe, Middlesex North

COMMITTEE ON MATERNAL WELFARE — Established 1941

- Raymond S Titus Suffolk, Chairman, Thomas Almy,
Bristol South, Edward P Bagg, Hampden, James M
Baty, Middlesex South, Stewart H Clifford, Middle-
sex South, Ralph E Cole, Middlesex North, Robert
L DeNormandie, Suffolk, Arthur F G Edgewood,
Hampden, Daniel J Ellison, Middlesex North,
Arthur M Kimberly, Worcester, Benjamin Lambert,
Middlesex North, Florence L McKay, Suffolk,
Joseph C Merriam, Middlesex South, Robert T
Moulton, Essex South, Joseph W O'Connor, Wor-
cester, Louis E Phaneuf, Suffolk, Warren R Sisson,
Suffolk, Richard M Smith, Suffolk, Richard J
Williams, Essex South

MEDICAL ADVISORY COMMITTEE TO REGIONAL OPA —
Established 1943

- Joseph Garland, Suffolk, Chairman, F Gorham Brigham,
Norfolk (interim appointment), Clifford L Derick,
Middlesex South, Loring Grimes, Essex South,
Franklin W White, Suffolk

MILITARY POSTGRADUATE COMMITTEE — Established 1942

- W Richard Ohler, Norfolk, Chairman, Chester S Keefer,
Suffolk, Gordon M Morrison, Middlesex South,
Frank R Ober, Suffolk, Leroy E Parkins, Suffolk,
Samuel H Proger, Norfolk

PHYSICAL MEDICINE — Established 1945

- Arthur L. Watkins, Middlesex South, Chairman, Ralph
M Chambers, Bristol North, Franklin P Lowry,
Middlesex South, Robert B Osgood, Suffolk, Henry
A. Tadgell, Hampshire

COMMITTEE ON POSTWAR PLANNING — Established 1944

- Howard F Root, Suffolk, Chairman, Leroy E Parkins,
Suffolk, Secretary, Arthur W Allen, Suffolk, Edward
P Bagg, Hampden, Elmer S Bagnall, Essex North
(interim appointment), George Ballantyne, Wor-
cester, Charles F Branch, Suffolk, C Sidney Burtwell,
Norfolk, Allan M Butler, Suffolk, Nathaniel W
Faxon, Suffolk, Vlado A Getting, Middlesex South,
G Philip Grabfield, Suffolk, Frederick S Hopkins,
Hampden, Chester M Jones, Suffolk, Eugene M
Landis, Middlesex South, Leland S McKittrick,
Suffolk, James Howard Means, Suffolk, Robert N
Nye, Suffolk, Frank R Ober, Suffolk, W Richard
Ohler, Norfolk, Walter G Phippen, Essex South,
Merrill C Sosman, Suffolk, Michael A. Tighe,
Middlesex North, Charles F Wilinsky, Suffolk

SUBCOMMITTEES OF THE COMMITTEE ON POSTWAR
PLANNING

(The Chairman and Secretary of the Committee on Postwar
Planning are members *ex officio* of the subcommittees)

CO-ORDINATING ON EDUCATION — Established 1944

- Charles F Branch, Suffolk, Nathaniel W Faxon, Suffolk,
W Richard Ohler, Norfolk

HOSPITALS — Established 1944

- Arthur W Allen, Suffolk, Nathaniel W Faxon, Suffolk,
James W Manary, Suffolk, Clifton T Perkins,
Middlesex East, Charles F Wilinsky, Suffolk.

MEDICAL ECONOMICS — Established 1944

- Leland S McKittrick, Suffolk, Chairman, Allan M
Butler, Suffolk, Vlado A Getting, Middlesex South,
Merrill C Sosman, Suffolk

MEDICAL SCHOOLS — Established 1944

- Charles F Branch, Suffolk, C Sidney Burtwell, Norfolk,
Walter G Phippen, Essex South

ORGANIZATION — Established 1944

- Edward P Bagg, Hampden, George Ballantyne, Wor-
cester, Frederick S Hopkins, Hampden, Chester
M Jones, Suffolk, James Howard Means, Suffolk,
Frank R Ober, Suffolk, Joseph W O'Connor, Wor-
cester, Francis J Steele, Worcester, Michael A
Tighe, Middlesex North

POSTGRADUATE EDUCATION — Established 1944

- W Richard Ohler, Norfolk, Chairman, Vlado A Getting,
Middlesex South, G Philip Grabfield, Suffolk,
Edward G Huber, Middlesex South, Lewis M
Hurxthal, Suffolk, Charles J Kickham, Norfolk,
Eugene M Landis, Middlesex South, Charles G
Mixer, Suffolk, Robert N Nye, Suffolk, Frank R
Ober, Suffolk, Joseph W O'Connor, Worcester,
Samuel H Proger, Norfolk, Harry C Solomon,
Suffolk.

SUBCOMMITTEES OF THE COMMITTEE ON PUBLIC RELATIONS

LABOR AND INDUSTRY — Established 1945

Daniel B Reardon, Norfolk South, Chairman, George J Connor, Essex North, Daniel J Ellison, Middlesex North, John Fallon, Worcester, Michael A Tighe, Middlesex North

COMMITTEE TO MEET WITH THE MEDICAL ADVISORY COMMITTEE OF THE INDUSTRIAL ACCIDENT BOARD — Established 1942

Daniel J Ellison, Middlesex North, Chairman, Gordon M Morrison, Middlesex South, David D Scannell, Norfolk

POSTPAYMENT MEDICAL CARE — Established 1942

Daniel J Ellison, Middlesex North, Chairman, *Michael F Barrett*, Plymouth, James H Brewster, Bristol North, *James T Brosnan*, Worcester, *Lucien R Chaput*, Essex North, Joseph D Collins, Hampshire, Charles F Fasce, Berkshire, Patrick E Gear, Hampden, Loring Grimes, Essex South, *Francis T Janitzen*, Suffolk, Egon E Kattwinkel, Middlesex South, Howard M Kemp, Franklin, *William G LeBrecht*, Worcester North, *Wilfred L McKenzie*, Middlesex East, Harold E Perry, Bristol South, Daniel B Reardon, Norfolk South, *Harold F Rowley*, Harwich Port, Norman A Welch, Norfolk

PUBLIC INFORMATION — Established 1945

John Fallon, Worcester, Chairman, *Roger T Doyle*, Norfolk, Roy J Heffernan, Norfolk, Howard F Root, Suffolk, Richard M Smith, Suffolk, Ralph R Stratton, Middlesex East, Michael A Tighe, Middlesex North, Roy J Ward, Worcester

TAX-SUPPORTED MEDICAL CARE — Established 1940

John J Dumphy, Worcester, Chairman, Frederick S Hopkins, Hampden, Albert A Hornor, Suffolk, William J Pelletier, Franklin, Frank W Snow, Essex North

COMMITTEE ON POSTWAR LOAN FUND — Established 1945

George Leonard Schadt, Hampden, Chairman, Eliot Hubbard, Jr., Middlesex South, Charles C Lund, Suffolk, Albert E Parkhurst, Essex South, Michael A Tighe, Middlesex North

COMMITTEE ON REHABILITATION — Established 1941

Joseph H Shortell, Suffolk, Chairman, Benjamin F Andrews, Worcester, Ralph M Chambers, Bristol North, William M Collins, Middlesex North, John Fallon, Worcester, *James J Regan*, Suffolk, Arthur L Watkins, Middlesex South

COMMITTEE TO CONSIDER EXPERT TESTIMONY — Established 1936

Frank R Ober, Suffolk, Chairman, Carl Bearse, Norfolk, William J Brickley, Suffolk, David Cheever, Suffolk, Francis P McCarthy, Norfolk

COMMITTEE TO MAKE RECOMMENDATIONS AS TO FUTURE DIRECTORS OF THE BLUE SHIELD — Established 1945

Leland S McKistrick, Suffolk, Chairman (Term expires May, 1949), *Elliott P Joslin*, Suffolk (Term expires May, 1947), Peirce H Leavitt, Plymouth (Term expires May, 1950), Donald Munro, Suffolk (Term expires May, 1946), *George Gilbert Smith*, Suffolk (Term expires May, 1948)

COMMITTEE TO MEET WITH THE MASSACHUSETTS HOSPITAL ASSOCIATION — Established 1940

Walter G Phippen, Essex South, Chairman, *Edward A Adams*, Worcester North, John Fallon, Worcester, Edwin D Gardner, Bristol South, Frederic Hagler, Hampden, Albert E Parkhurst, Essex South

COMMITTEE TO STUDY POSSIBLE REVISION OF BY-LAWS AS THEY RELATE TO THE ELECTION OF FELLOWS — Established 1945

Charles J Kickham, Norfolk, Chairman, William A R Chapin, Hampden, C Bertram Gay, Worcester North, Peirce H Leavitt, Plymouth, Donald Munro, Suffolk, Daniel B Reardon, Norfolk South, Michael A Tighe, Middlesex North

WAR PARTICIPATION COMMITTEE — Established 1943

Guy L Richardson, Essex North, Chairman, Carl Bearse, Norfolk, Harold G Giddings, Middlesex South, Walter H Pulsifer, Plymouth, Ralph R Stratton, Middlesex East, Michael A Tighe, Middlesex North

TWENTY-FIVE VOTING MEMBERS IN MASSACHUSETTS HOSPITAL SERVICE, INC — Established 1939

Benjamin H Alton, Worcester, *Gerardo M Balboni*, Suffolk, *Laurence D Chapin*, Hampden, *Lucien R Chaput*, Essex North, Hilbert F Day, Middlesex South, *Augustus W Dudley*, Middlesex South, John Fallon, Worcester, *George K Fenn*, Essex South, *Joseph E Flynn*, Middlesex South, Archibald R Gardner, Middlesex North, Henry W Godfrey, Middlesex South, Albert A Hornor, Suffolk, *John H Lambert*, Middlesex North, Alexander A Levi, Middlesex South, Joseph C Merriam, Middlesex South, Donald Munro, Suffolk, Albert E Parkhurst, Essex South, Helen S Pittman, Suffolk, Allen G Rice, Hampden, *Arthur T Ronan*, Norfolk, Frank W Snow, Essex North, George L Steele, Hampden, Ralph R Stratton, Middlesex East, *John E Talbot*, Worcester, *Edward L Young*, Norfolk

REPRESENTATIVES TO THE MASSACHUSETTS CENTRAL HEALTH COUNCIL

James W Bunce, Berkshire, *Merrill E Champion* (Suffolk), George D Henderson, Hampden, William D Kinney, Barnstable, *Robert B Orgood*, Suffolk, Roy J Ward, Worcester

REPRESENTATIVE TO MENTAL HEALTH FOR VICTORY ORGANIZATION

Abraham Myerson, Norfolk

REPRESENTATIVE TO THE HOSPITAL COUNCIL OF BOSTON FOR THE YEAR 1945

William E Browne, Suffolk

REPRESENTATIVE TO THE MASSACHUSETTS COMMITTEE FOR NURSES PROCUREMENT AND ASSIGNMENT SERVICE

Dwight O'Hara, Middlesex South

REPRESENTATIVE TO THE LEGISLATIVE COMMITTEE OF THE MASSACHUSETTS GENERAL HEALTH COUNCIL

William E Browne, Suffolk

REPRESENTATIVE FROM THE MASSACHUSETTS MEDICAL SOCIETY TO THE MASSACHUSETTS NURSING COUNCIL FOR WAR SERVICE

David D Scannell, Norfolk

REPRESENTATIVE FROM THE MASSACHUSETTS MEDICAL SOCIETY TO A PROFESSIONAL ADVISORY COMMITTEE TO BE ORGANIZED BY THE DIVISION OF VOCATIONAL REHABILITATION OF STATE DEPARTMENT OF EDUCATION FOR PURPOSE OF ESTABLISHING A PROGRAM ON PHYSICAL RESTORATION

Joseph H Shortell, Suffolk

REPRESENTATIVES TO THE NEW ENGLAND MEDICAL COUNCIL

Dwight O'Hara, Middlesex South, Allen G Rice, Hampden, Michael A Tighe, Middlesex North

DELEGATES AND ALTERNATES TO THE HOUSE OF DELEGATES OF THE AMERICAN MEDICAL ASSOCIATION, FOR 1945-1946

DELEGATES

ALTERNATES

June 1, 1944, to June 1, 1946

David D Scannell, Norfolk Elmer S Bagnall, Essex North
Dwight O'Hara, Middlesex Ernest L Hunt, Worcester
South
Charles E Mongan, Middle- Patrick E Gear, Hampden
sex South
Walter G Phippen, Essex John I B Vail, Barnstable
South

June 1, 1945, to June 1, 1947

Charles J Kickham, Norfolk John Fallon, Worcester
Leland S McKittick, Suffolk Patrick J Sullivan, Berk-
shire

COUNCILORS FOR 1945-1946

(ELECTED BY THE DISTRICT MEDICAL SOCIETIES AT THEIR ANNUAL MEETINGS, APRIL 15 TO MAY 15, 1945)

The initials *E C* following the name of a councilor indicate that he is a member of the Executive Committee and *A E C* that he is an alternate member of the Executive Committee *M N C* that he is a member of the Committee on Nominations and *A M N C* that he is an alternate member of the Committee on Nominations *Leg C* that he is a member of the Committee on Legislation *P R C* that he is a member of the Committee on Public Relations *P P* that a member is a councilor by virtue of his office as president of a district society and so vice-president of the general society *C* by virtue of his office as chairman of a standing committee *Sec* by virtue of his office as secretary of a district society and *Ex Pres* by virtue of being a past president.

BARNSTABLE

J N Kelly, Orleans, River Rd, V P
P M Butterfield, Harwich, E C, A M N C
C H Keene, Chatham, Seaview St.
J G Kelley, Pocasset, Barnstable County Sanatorium,
Sec, Leg C
W D Kinney, Osterville, A E C, M N C, P R C

BERKSHIRE

T H Nelligan, Pittsfield, 184 North St, V P
D N Beers, Pittsfield, 74 North St, Sec.
I S F Dodd, Pittsfield, 34 Fenn St, E C
C F Fasse, Pittsfield, 311 North St, A M N C
C F Kernan, Pittsfield, 184 North St, Leg C
J F McLaughlin, Adams, 25 Park St
Solomon Schwager, Pittsfield, 246 North St
Helen M Scoville, Pittsfield, House of Mercy Hospital
P J Sullivan, Dalton, 471 Main St, A E C, M N C,
P R C

BRISTOL NORTH

W M Stobbs, Attleboro, 63 Bank St., V P
W H Allen, Mansfield, 70 North Main St., E C,
M N C
J H Brewster, Attleboro, 178 South Main St, P R C
R M Chambers, Taunton, Taunton State Hospital,
A E C, Leg C
W J Morse, Attleboro, 34 Sanford St, Sec
J L Murphy, Taunton, 23 Cedar St., A M N C

BRISTOL SOUTH

J C Corrigan, Fall River, 422 North Main St, V P
C W Blood, Fall River, 82 New Boston Rd, A E C
R B Butler, Fall River, 278 North Main St., A M N C
E F Cody, New Bedford, 105 South Sixth St, M N C
J E Fell, Fall River, 441 Stanley St. Sec.
J A Fournier, Fall River, 11 Choate St
E D Gardner, New Bedford, 150 Cottage St, E C
F M Howes, New Bedford, 135 Cottage St
H E Perry, New Bedford, 159 Cottage St
I N Tilden, Mattapoisett, Barstow St
C C Trapp, New Bedford, 416 County St
Henry Wardle, Fall River, 173 Purchase St

ESSEX NORTH

P J Look, Andover, 115 Main St, V P
E S Bagnall, Groveland, 281 Main St., Ex-Pres
R V Baketel, Methuen, 7 Hampshire St.

G J Connor, Haverhill 81 Merrimack St.
Elizabeth Councilman, Newburyport, 83 High St
H A Fenton, Lawrence, 36 Winthrop Ave
E H Ganley, Methuen, 251 Broadway, Leg C
H R Kurth, Lawrence, 57 Jackson St, Sec, P R C
J G Miller, Lawrence, 80 East Haverhill St
R J Neil, Methuen, 255 Broadway
R C Norris, Methuen, 247 Broadway, A E C,
A M N C
G L Richardson, Haverhill, 94 Emerson St, M N C
F W Snow, Newburyport, 24 Essex St, E C
C F Warren, Amesbury, 1 School St

ESSEX SOUTH

W R Irving, Gloucester, 35 Middle St., V P
Bernard Appel, Lynn, 281 Ocean St, A E C
H A Boyle, Middleton, Essex Sanatorium
D S Clark, Salem, 2 Oliver St
C L Curtis, Salem, 10 Federal St
R E Foss, Peabody, 125 Main St
Loring Grimes, Swampscott, 84 Humphrey St., P R C
P P Johnson, Beverly, 1 Monument Sq, A M N C
H M Lowd, Swampscott, 90 Burill St
B B Mansfield, Ipswich, 4 Green St
A E Parkhurst, Beverly, Monument Sq
O S Pettingill, Middleton, Essex Sanatorium
W G Phippen, Salem, 31 Chestnut St, Ex-Pres, E C
E D Reynolds, Danvers, 48 High St.
C S Rust, Gloucester, 48 Pleasant St
T L Shipman, Lynn, 920 Western Ave, C
H D Stebbins, Salem, 26 Chestnut St, Sec
P E Tivnan, Salem, 70 Washington St., M N C
C F Twomey, East Lynn, 80 Ocean St.
C A Worthen, Lynn, 19 Park St, Leg C

FRANKLIN

K H Rice, South Deerfield, 141 Main St., V P
H L Craft, Ashfield, Sec
H M Kemp, Greenfield, 42 Franklin St, A M N C,
Leg C
J E Moran, Greenfield, 31 Federal St, A E C, P R C
W J Pelletier, Turners Falls, 113 Ave A, E C, M N C

HAMPTON

M F Hosmer, Longmeadow, Office Springfield, 20 Maple
St, V P
F H Allen, Holyoke, 16 Fairfield St
E P Bagg, Holyoke, 207 Elm St., A E C
J M Birnie, Springfield, 146 Chestnut St, Ex-Pres
H F Byrnes, Springfield, 6 Chestnut St, A M N C
W A R Chapin, Springfield, 121 Chestnut St, E C
J L Chereskin, Springfield, 333 Bridge St
A J Douglas, Westfield, 93 Elm St
E C Dubois, Springfield, 174 Buckingham St
G L Gabler, Holyoke, 4 Bullard Ave
P E Gear, Holyoke, 188 Chestnut St, P R C
Frederic Hagler, Springfield, 20 Maple St
G D Henderson, Holyoke, 176 Chestnut St
F S Hopkins, Springfield, 146 Chestnut St
Charles Jurist, Springfield, 70 Chestnut St.
M M Pearson, Ware, 19 Pleasant St
A G Rice, Springfield, 146 Chestnut St, M N C
A H Riordan, Indian Orchard, 147 Oak St, Leg C
G L Schadt, Springfield, 44 Chestnut St., Ex-Pres
J A Seaman, Longmeadow, Office Springfield, 20 Maple
St
G C Steele, West Springfield, 39 Upper Church St, Sec.
G L Steele, Springfield, 20 Maple St

HAMPSHIRE

A N Ball, Northampton, State Hospital, V P Leg C
J D Collins, Northampton, 187 Main St, E C,
A M N C
W M Dobson, Northampton Veterans Administration
Facility, A E C, P R C
L B Pond, Easthampton, 115 Main St., E C
Mary P Snook, Worthington, Sec
H A Taggell, Belchertown, Belchertown State School,
M N C

MIDDLESEX EAST

J L Anderson, Reading, 53 Woburn St, V P
 R M Burgoyne, Winchester, 15 Washington St
 Richard Dutton, Wakefield, 33 Avon St, A E C
 E M Halligan, Reading, 37 Salem St, E C, A M N C
 D L Joyce, Woburn, 269 Main St
 R W Dayton, Melrose 76, 8 Porter St, Sec
 M J Quinn, Winchester, 44 Church St, P R C
 W F Regan, Winchester, 101 High St.
 R R Stratton, Melrose 76, 538 Lynn Fells Parkway,
 M N C, C
 J M Wilcox, Woburn, 6 Bennett St, Leg C

MIDDLESEX NORTH

A E Shaw, Lowell, 386 Andover St, V P
 J J Cassidy, Lowell, 9 Central St, M N C
 H R Coburn, Lowell, 202 Merrimack St
 W M Collins, Lowell, 174 Central St, A E C,
 A M N C
 D J Ellison, Lowell, 8 Merrimack St, P R C
 A R Gardner, Lowell, 16 Shattuck St., Leg C
 B D Leahy, Lowell, 9 Central St, Sec
 W F Ryan, Lowell, 219 Central St, E C
 M A Tighe, Lowell, 9 Central St, Secretary

MIDDLESEX SOUTH

H G Giddings, Newton Centre, Office Boston 16, 270
 Commonwealth Ave, V P, E C
 E W Barron, Malden 48, Office Boston, 20 Ash St
 W B Bartlett, Concord, 28 Monument St
 Harris Bass, Everett 49, 351 Broadway
 J M Baty, Belmont, Office Brookline 46, 1101 Beacon
 St
 J D Bennett, West Somerville 44, 72 College Ave
 E H Bigelow, Framingham, Hotel Kendall, Ex-Pres
 W O Blanchard, Newton 58, 465 Centre St
 G F H Bowers, Newton Highlands 61, 156 Woodward
 St.
 Alice M Broadhurst, Watertown 72, 259 Mt Auburn St
 Madeline R Brown, Cambridge, Office Boston 16, 264
 Beacon St
 R N Brown, Malden 48, 621 Main St
 R W Buck, Waban, Office Boston 15, 5 Bay State Rd
 E J Butler, Cambridge, 25 Garden St
 J F Casey, Allston, Office Boston 15, 475 Commonwealth
 Ave
 C W Clark, Newtonville 60, 363 Walnut St
 J A Daley, Natick, 36 Pond St
 H F Day, Cambridge, 34 Kirkland St
 C L Derick, Newton Highlands, Office Boston 15, 412
 Beacon St
 J G Downing, Newton, Office Boston 15, 520 Common-
 wealth Ave
 C W Finnerty, West Somerville 44, 5 Pearson Rd
 H Q Gallupe, Waltham 54, 751 Main St
 F W Gay, Malden 48, 20 Park St
 V A Getting, Belmont, Office Boston 8, 546 State House
 H W Godfrey, Auburndale 66, 14 Hancock St
 J L Golden, Medford 55, 86 Forest St
 A D Guthrie, Medford 55, 408 Salem St
 Eliot Hubbard, Jr, Cambridge, 29 Highland St,
 Treasurer
 A M Jackson, Everett 49, 512 Broadway, A E C
 F R Jouett, Cambridge, 1 Craigie St
 E E Kattwinkel, West Newton 65, 65 Sterling St.
 A A Levi, Newton, Office Boston 15, 481 Beacon St,
 Sec
 F P Lowry, Newton 58, 313 Washington St
 A N Makechnie, Cambridge, 14 Upland St
 P H Means, Cambridge, 1 Waterhouse St.
 J C Merriam, Framingham, 198 Union Ave, A M N C
 Dudley Merrill, Cambridge, 51 Brattle St.
 C E Mongan, Somerville 43, 24 Central St, Ex-Pres
 G M Morrison, Waban, Office Boston 15, 520 Common-
 wealth Ave, P R C
 J P Nelligan, Cambridge, 2336 Massachusetts Ave
 E J O'Brien, Jr, Newton, Office Boston 16, 270 Com-
 monwealth Ave, Leg C
 Dwight O'Hara, Waltham, Office Boston 15, 416 Hunt-
 ington Ave, President-Elect, M N C, C

Fabyan Packard, Belmont, Office Boston, Soldiers' Field
 L G Paul, Newton Centre, Office Boston 16, 270 Com-
 monwealth Ave
 T E Reilly, Marlboro, 6 Newton St.
 S H Remick, Waltham 54, 735 Trapelo Rd
 Max Ritvo, Newton, Office Boston 15, 485 Commos-
 wealth Ave
 E H Robbins, Somerville 43, 334 Broadway
 M J Schlesinger, Newton, Office Boston 15, 330 Brook-
 line Ave
 E W Small, Belmont 78, 68 Leonard St
 H P Stevens, Cambridge, 1 Craigie St
 K J Tillotson, Waverley 79, McLean Hospital
 A B Toppan, Watertown 72, 289 Mt Auburn St.
 J E Vance, Natick, Office Boston 15, 29 Bay State Rd.
 Fresenius Van Nüys, Weston 93, 338 Boston Post Rd
 C F Walcott, Cambridge, 81 Sparks St
 A L Watkins, Arlington, Office Boston 14, Massa-
 chusetts General Hospital
 B M Wein, Newton, Office Boston 15, 471 Common-
 wealth Ave
 B S Wood, Weston, Office Waltham 54, 751 Main St.
 Alfred Worcester, Waltham 54, 314 Bacon St, Ex Pres.
 Hovhannes Zovickian, Watertown 72, 528 Mt Auburn St

NORFOLK

D S Luce, Canton, 553 Washington St, V P
 C E Allard, Dorchester, 428 Columbia Rd, A M N C.
 B E Barton, West Roxbury 32, 10 Richwood St, Sec.
 Carl Bearse, Boston 15, 483 Beacon St
 Arthur Berk, Brookline, Office Boston 16, 270 Com-
 monwealth Ave
 M I Berman, Dorchester, 1071A Blue Hill Ave
 J H Cauley, Dorchester, 8 Carruth St
 D J Collins, Norwood, 100 Day St
 William Dameshek, Brookline, Office Boston 15, 111
 Bay State Rd
 G L Doherty, West Roxbury, Office Boston 15, 466
 Commonwealth Ave
 Albert Ehrenfried, Brookline, Office Boston 15, 520
 Beacon St, M N C
 J J Elliott, Roslindale 31, 4258 Washington St
 H M Emmons, Needham, Office Boston 15, 354 Com-
 monwealth Ave
 Susannah Friedman, Roxbury, Office Boston 15, 485
 Commonwealth Ave
 B A Godvin, Jamaica Plain, Office Boston 15, 483
 Beacon St
 J B Hall, Roxbury 19, 108 Dudley St.
 H B Harris, East Milton, Office Dorchester, 487 Co-
 lumbia Rd
 R J Heffernan, Jamaica Plain, Office Brookline 46,
 1101 Beacon St, C
 P J Jakmauh, Milton, Office South Boston 27, 509
 Broadway
 I R Jankelson, Jamaica Plain, Office Boston 15, 483
 Beacon St.
 C J Kickham, Brookline, Office Boston 15, 524 Com-
 monwealth Ave, E C
 C J E Kickham, Jamaica Plain, Office Brookline 46,
 1101 Beacon St
 H M Landesman, Roxbury, Office Boston, 429 Marl-
 borough St.
 C M Lydon, Dorchester, 276 Bowdoin St
 D L Lynch, Roslindale, Office Boston, 245 State St
 F P McCarthy, Milton, Office Boston 15, 371 Com-
 monwealth Ave
 H L McCarthy, West Roxbury, Office Boston 15, 479
 Beacon St, Leg C
 R T Monroe, Brookline, Office Boston 16, 270 Com-
 monwealth Ave, C
 F J Moran, Dedham, 395 Washington St
 Hyman Morrison, Roxbury, Office Boston 15, 483
 Beacon St
 D J Mullane, Jamaica Plain 30, 776 Centre St
 Abraham Myerson, Brookline, Office Boston 15, 475
 Commonwealth Ave
 J J O'Connell, Dorchester, 1061 Dorchester Ave
 W R Ohler, Jamaica Plain, Office Boston 15, 319 Long-
 wood Ave.
 G W Papen, Brookline, Office Boston, 31 Milk St.

H C Petterson, West Roxbury, Office Boston 15, 29 Bay State Rd
 Frederick Reis, Jamaica Plain, Office Boston 15, 416 Huntington Ave
 S A Robins, Roxbury, Office Boston 15, 636 Beacon St.
 D D Scannell, Jamaica Plain, Office Boston 15, 475 Commonwealth Ave
 J A Seth, Milton, Office Boston 15, 47 Bay State Rd
 L A Sieracki, Norwood, 71 Winter St
 Kathlyne S Snow, Jamaica Plain, Office Boston 15, 466 Commonwealth Ave
 S L Skvirsky, Chestnut Hill, Office Boston, 336 State House
 J W Spellman, Chestnut Hill, Office Brookline 46, 1101 Beacon St
 M H Spellman, Jamaica Plain, Office Boston 15, 475 Commonwealth Ave
 J P Treanor, Jr, Jamaica Plain, Office Brookline 46, 1101 Beacon St.
 W J Walton, Dorchester, 106 Bowdoin St
 S H Weiner, Roxbury, Office Boston 15, 524 Commonwealth Ave
 N A Welch, West Roxbury, Office Boston 15, 520 Commonwealth Ave, P R C, Assistant Treasurer
 Louis Wolff, Brookline, Office Boston 16, 270 Commonwealth Ave

NORFOLK SOUTH

F W Crawford, Holbrook, 98 North Franklin St, V P
 C S Adams, Wollaston 70, 62 Brooks St.
 F A Bartlett, Wollaston 70, 308 Beale St.
 D L Belding, Hingham, Office Boston 18, 80 East Concord St, Leg C
 Harry Braierman, Quincy 69, 43 School St.
 Frederick Hinchliffe, Cohasset, 117 South Main St
 E K Jenkins, South Braintree 85, Norfolk County Hospital, Sec.
 J E Knowlton, Quincy 69, 579 Hancock St, A M N C
 N R Pillsbury, South Braintree, Norfolk County Hospital, A E C, P R C
 D B Reardon, Quincy, 1186 Hancock St., E C, M N C

PLYMOUTH

P B Kelly, Plymouth, 63 Court St., V P
 C H King, Duxbury, Cedar St.
 P H Leavitt, Brockton, 129 West Elm St, E C
 C D McCann, Brockton, 12 Cottage St., P R C
 R C McLeod, Brockton, Goddard Hospital, Sec.
 J J McNamara, Brockton, 231 Main St, Leg C
 C A Moore, Brockton, 167 Newbury St., A M N C
 B H Peirce, South Hanson, Plymouth County Hospital, M N C
 E L Perry, Middleboro, 39 Oak St.
 W H Pulsifer, Whitman, 26 Park Ave

SUFFOLK

Donald Munro, Boston 18, 818 Harrison Ave., V P
 A W Allen, Boston 16, 266 Beacon St, C
 J W Bartol, Boston, 1 Chestnut St, Ex-Pres
 W H Blanchard, Chelsea 50, Soldiers' Home
 W J Brickley, Boston 15, 524 Commonwealth Ave.
 W E Browne, Boston 15, 587 Beacon St, Leg C
 A M Butler, Boston 14, Massachusetts General Hospital
 A J A Campbell, Boston 15, 520 Commonwealth Ave, E C
 David Cheever, Boston 16, 193 Marlborough St.
 Pasquale Costanza, East Boston 28, 238 Maverick St
 N W Faxon, Boston 14, Massachusetts General Hospital
 Jacob Fine, Boston 15, 330 Brookline Ave
 Reginald Fitz, Boston 15, 319 Longwood Ave., President
 Somers Fraser, Boston 15, 395 Commonwealth Ave
 Maurice Fremont-Smith, Boston 15, 12 Hereford St.
 Channing Frothingham, Boston, Office Jamaica Plain 30, 1153 Centre St, Ex-Pres
 Joseph Garland, Boston 16, 266 Beacon St
 R L Goodale, Boston 16, 330 Dartmouth St., Sec
 F C Hall, Boston 15, 372 Marlborough St, C
 John Homans, Boston 16, 311 Beacon St
 A A Horner, Boston 15, 319 Longwood Ave, M N C, P R C

L M Hurxthal, Boston 15, 605 Commonwealth Ave
 C S Keefer, Boston 18, 65 East Newton St
 H A Kelly, Winthrop 52, 200 Pleasant St
 R I Lee, Boston 16, 264 Beacon St, Ex-Pres
 C C Lund, Boston 15, 319 Longwood Ave
 P E Meltzer, Boston 15, 20 Charlesgate West
 W J Mixer, Boston 15, 319 Longwood Ave, Vice-President
 H L Musgrave, Revere 51, 622 Beach St
 H F Newton, Boston 15, 319 Longwood Ave, C
 R N Nye, Boston 15, 8 Fenway
 F R Ober, Boston 16, 234 Marlborough St., Ex-Pres
 F W O'Brien, Boston 15, 465 Beacon St.
 J P O'Hare, Boston 15, 520 Commonwealth Ave.
 L E Parkins, Boston 15, 12 Bay State Rd
 L E Phaneuf, Boston 16, 270 Commonwealth Ave
 Helen S Pittman, Boston 16, 264 Beacon St.
 J H Pratt, Boston 11, 30 Bennet St
 W H Robey, Boston 16, 202 Commonwealth Ave., Ex-Pres
 H F Root, Boston 15, 81 Bay State Rd, A E C
 R M Smith, Boston 16, 330 Dartmouth St., C
 M C Sosman, Boston 15, 721 Huntington Ave
 E F Timmins, South Boston 27, 527 Broadway
 J J Todd, Boston 15, 587 Beacon St.
 S N Vose, Boston 15, 29 Bay State Rd
 Conrad Wesselhoeft, Boston, 315 Marlborough St., A M N C
 C F Wilinsky, Boston 15, 330 Brookline Ave

WORCESTER

C R Abbott, Clinton, 60 Walnut St., V P
 B H Alton, Worcester, 27 Elm St
 B F Andrews, Worcester, 36 Pleasant St
 A W Atwood, Worcester, 390 Main St
 George Ballantyne, Worcester, 27 Elm St.
 Gordon Berry, Worcester, 36 Pleasant St
 F P Bousquet, Worcester, 390 Main St
 W P Bowers, Clinton, 264 Chestnut St, Ex-Pres
 E J Crane, Holden, Armington Lane
 J J Dumphy, Worcester, 390 Main St, A E C
 W J Elliott, Worcester, 119 Belmont St
 J M Fallon, Worcester, 390 Main St, P R C
 L M Felton, Worcester, 36 Pleasant St, Leg C
 J V Gallagher, Milford, 224 Main St
 L P Leland, Worcester, 36 Pleasant St., Sec
 W F Lynch, Worcester, 390 Main St., M N C
 J C McCann, Worcester, 390 Main St.
 A E O'Connell, Worcester, 390 Main St
 H L Paine, North Grafton, Grafton State Hospital
 R S Perkins, Worcester, 10 Hackfeld Rd, A M N C
 O H Stansfield, Worcester, 36 Pleasant St.
 T L Story, Southbridge, 17 Maple St
 J C Sullivan, Webster, 18 Negus St
 R J Ward, Worcester, 9 Bellevue St., C
 R P Watkins, Worcester, 332 Main St.
 B C Wheeler, Worcester, 27 Elm St., E C
 S B Woodward, Worcester, 58 Pearl St, Ex-Pres

WORCESTER NORTH

R F Bachmann, Fitchburg, 910 Main St., V P
 H C Arey, Gardner, 66 Parker St.
 D B Cheetham, Athol, 164 Exchange St, Leg C
 C B Gay, Fitchburg, 62 Day St, E C
 G P Keaveny, Fitchburg, 62 Day St., A M N C, A E C
 J V McHugh, Leominster, 100 Main St., P R C
 J G Simmons, Fitchburg, 30 Myrtle Ave, Sec

CENSORS FOR 1945-1946

BARNSTABLE

W D Kinney, Osterville, *supervisor*
 E F Curry, Sagamore
 C E Harris, Hyannis
 J I B Vail, Hyannis
 D H Hiebert, Provincetown

BERKSHIRE

P J Sullivan, Dalton, *supervisor*
 I S F Dodd, Pittsfield
 A C England, Pittsfield
 M M Brown, North Adams
 W T Frawley, Pittsfield

BRISTOL NORTH

W H Allen, Mansfield, *supervisor*
 J L Murphy, Taunton
 A J Leddy, Taunton
 L E Butler, Taunton
 J H Brewster, Attleboro

BRISTOL SOUTH

Henry Wardle, Fall River, *supervisor*
 E A McCarthy, Fall River
 F M Howes, New Bedford
 W F MacKnight, Fall River
 C C Persons, New Bedford

ESSEX NORTH

R V Baketel, Methuen, *supervisor*
 L C Peirce, Newburyport
 P W Blake, Andover
 C H Birdsall, Haverhill
 C R Hines, Amesbury

ESSEX SOUTH

A E Parkhurst, Beverly, *supervisor*
 J C Adams, Salem
 R A Harpin, Lynn
 I B Hull, Gloucester
 W C Inman, Danvers

FRANKLIN

J E Moran, Greenfield, *supervisor*
 P N Freeman, Greenfield
 H R Mahar, Orange
 F W Dean, Northfield
 C R Vinal, Turners Falls

HAMPDEN

Frederic Hagler, Springfield, *supervisor*
 A F G Edgelow, Springfield
 J M Gilchrist, Springfield
 G D Henderson, Holyoke
 John Pallo, Westfield

HAMPSHIRE

L B Pond, Easthampton, *supervisor*
 M E Cooney, Northampton
 T F Corriden, Northampton
 J E Hayes, Northampton
 C H Wheeler, Haydenville

MIDDLESEX EAST

M J Quinn, Winchester, *supervisor*
 J H Fay, Melrose
 C E Montague, Wakefield
 S H Moses, Winchester
 C R Baisley, Reading

MIDDLESEX NORTH

W F Ryan, Lowell, *supervisor*
 F R Brady, Lowell
 R C Stewart, Lowell
 H L Leland, Lowell
 J D Sweeney, Lowell

MIDDLESEX SOUTH

H Q Gallupe, Waltham, *supervisor*
 A H Makechnie, Cambridge
 H W Thayer, Newtonville
 E H Robbins, Somerville
 J E Dodd, Framingham

NORFOLK

Hyman Morrison, Roxbury, *supervisor*
 C J Kickham, Brookline
 C E Allard, Dorchester
 H Allan Novack, Brookline
 Kathlyne S Snow, Jamaica Plain

NORFOLK SOUTH

C S Adams, Wollaston, *supervisor*
 R O Gilmore, Quincy
 R F Ross, South Braintree
 R R Ryan, South Weymouth
 W L Sargent, Quincy

PLYMOUTH

E L Perry, Middleboro, *supervisor*
 D W Pope, Brockton
 J H Dunn, Rockland
 J A Pettey, Brockton
 R E Swenson, Plymouth

SUFFOLK

J H Pratt, Boston, *supervisor*
 H T Hutchins, Boston
 A J A Campbell, Boston
 W E Browne, Boston
 E F Timmins, South Boston.

WORCESTER

B C Wheeler, Worcester, *supervisor*
 H K Spangler, Worcester
 George Ballantyne, Worcester
 E J Crane, Holden
 W E Murphy, Worcester

WORCESTER NORTH

C B Gay, Fitchburg, *supervisor*
 F J Djerf, Fitchburg
 J W Mason, Ashburnham
 E B Hopkins, Ayer
 W E Currier, Leominster

VICE-PRESIDENTS OF THE MASSACHUSETTS
 MEDICAL SOCIETY (*Ex-Officio*)
 FOR 1945-1946

PRESIDENTS OF DISTRICT MEDICAL SOCIETIES
 (Arranged according to seniority of fellowship
 in the Massachusetts Medical Society)

MIDDLESEX NORTH — Adam E Shaw, Lowell
 NORFOLK — Dean S Luce, Canton
 MIDDLESEX SOUTH — Harold G Giddings, Newton Centre
 NORFOLK SOUTH — Frank W Crawford, Holbrook
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 SUFFOLK — Donald Munro, Boston
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 WORCESTER NORTH — Rudolf F Bachmann, Fitchburg
 BRISTOL SOUTH — John C Corrigan, Fall River
 PLYMOUTH — P Brooks Kelly, Plymouth
 BARNSTABLE — Joseph N Kelly, Orleans

COMMISSIONERS OF TRIAL FOR 1945-1946

BARNSTABLE — F O Cass, Provincetown
 BERKSHIRE — J B Thomes, Pittsfield
 BRISTOL NORTH — J W Cook, Mansfield
 BRISTOL SOUTH — A C Lewis, Fall River

ESSEX NORTH — F W Anthony, Haverhill
 ESSEX SOUTH — O C Blair, Lynn
 FRANKLIN — K W D Jacobus, Turners Falls
 HAMPDEN — F K Dutton, Springfield
 HAMPSHIRE — W M Dobson, Northampton
 MIDDLESEX EAST — I W Richardson, Wakefield
 MIDDLESEX NORTH — J F Boyle, Lowell
 MIDDLESEX SOUTH — H P Stevens, Cambridge
 NORFOLK — W J Walton, Dorchester
 NORFOLK SOUTH — F A Bartlett, Wollaston
 PLYMOUTH — J A Carriuolo, Brockton
 SUFFOLK — J R Torbert, Boston
 WORCESTER — W P Bowers Clinton
 WORCESTER NORTH — A P Lachance, Gardner

OFFICERS OF THE SECTIONS FOR 1946

ELECTED BY THE SECTIONS

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Chairman, Albert A Hornor, Boston, *vice-chairman*, Daniel J Ellison, Lowell, *secretary*, Francis C Hall, Boston

SECTION OF SURGERY

Chairman, Charles F Twomey, East Lynn, *secretary*, Alexander J A Campbell, Boston
Executive Committee — Stanley J G Nowak, Belmont and Boston (1 year), Edward L Young, Jr, Brookline and Boston (2 years), E Parker Hayden, Brookline and Boston (3 years)

SECTION OF PEDIATRICS

Chairman, Floyd R Smith, Pittsfield, *secretary*, Gerald N Hoeffel, Cambridge
Executive Committee — *Chairman*, Philip H Sylvester, Boston, James Marvin Baty, Belmont and Brookline, Leroy T Stokes, Haverhill

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SECTION OF RADIOLOGY

Chairman, George Levene, Chestnut Hill and Boston, *secretary*, Edward B D Neuhauser, Cambridge and Boston

SECTION OF PHYSIOTHERAPY

Chairman, Arthur L Watkins, Arlington and Boston, *secretary*, Howard Moore, Newton and Boston

SECTION OF DERMATOLOGY AND SYPHILOLOGY

Chairman, Bernard Appel, Lynn, *secretary*, Fenner A Chace, Fall River

SECTION OF ANESTHESIOLOGY

Chairman, Sidney C Wiggan, Waban and Jamaica Plain, *secretary*, Leo V Hand, Newton Highlands and Boston

OFFICERS OF THE DISTRICT MEDICAL SOCIETIES FOR 1945-1946

BARNSTABLE — *President*, Joseph N Kelly, Orleans, *vice-president*, Harold F Rowley, Harwich Port, *secretary*, Julius G Kelley, Pocasset, *treasurer*, Frank Travers, Barnstable, *librarian*, Carroll H Keene, Chatham, *executive counselor*, Paul M Butterfield, Harwich, *legislative counselor*, Julius G Kelley, Pocasset, *public-relations counselor*, William D Kinney, Osterville

BERKSHIRE — *President* Thomas H Nelligan, Pittsfield, *vice-president*, N Newall Copeland, Pittsfield, *secretary*, Daniel N Beers, Pittsfield, *treasurer*, Theodore W Jones, Pittsfield, *executive counselor*, Isaac S F Dodd, Pittsfield, *legislative counselor*, Clement F Kernan, Pittsfield, *public-relations counselor*, Patrick J Sullivan, Dalton

BRISTOL NORTH — *President*, William M Stobbs, Attleboro, *vice-president*, Joseph V Chatigny, Taunton, *secretary*, William J Morse, Attleboro, *treasurer*, Charles E Hoyer, Taunton, *executive counselor*, William H Allen, Mansfield, *legislative counselor*, Ralph M Chambers, Taunton, *public-relations counselor*, James H Brewster, Attleboro

BRISTOL SOUTH — *President*, John C Corrigan, Fall River, *vice-president*, S Perry Wilde, New Bedford, *secretary and treasurer*, James E Fell, Fall River, *executive counselor*, Edwin D Gardner, New Bedford

ESSEX NORTH — *President*, Percy J Look, Andover, *vice-president*, Guy L Richardson, Haverhill, *secretary*, Harold R Kurth, Methuen, *treasurer*, Lawrence Murphy, Newburyport, *executive counselor*, Frank W Snow, Newburyport, *legislative counselor*, Edward H Ganley, Methuen, *public-relations counselor*, Harold R Kurth, Methuen

ESSEX SOUTH — *President*, William R Irving, Gloucester, *vice-president*, John W Trask, Lynn, *secretary*, Henry D Stebbins, Marblehead, *treasurer*, Charles F Deering, Danvers, *executive counselor*, Walter G Phippen, Salem, *legislative counselor*, Charles A Worthen, Lynn, *public-relations counselor*, Loring Grimes, Lynn

FRANKLIN — *President*, Kenneth H Rice, South Deerfield, *vice-president*, John B Temple, Shelburne Falls, *secretary and treasurer*, Harry L Craft, Ashfield, *executive counselor*, William J Pelletier, Turners Falls, *legislative counselor*, Howard M Kemp, Greenfield, *public-relations counselor*, John E Moran, Greenfield

HAMPDEN — *President*, Merrill F Hosmer, Springfield, *vice-president*, Patrick E Gear, Holyoke, *secretary and treasurer*, George C Steele, West Springfield, *executive counselor*, William A R Chapin, Springfield, *legislative counselor*, Arthur Riordan, Indian Orchard, *public-relations counselor*, Patrick E Gear, Holyoke

HAMPSHIRE — *President*, Arthur N Ball, Northampton, *vice-president*, Elmer H Copeland, Northampton, *secretary and treasurer*, Mary P Snook, Worthington, *librarian*, Abbie M O'Keefe, Northampton, *executive counselor*, Joseph D Collins, Northampton, *legislative counselor*, Arthur N Ball, Northampton, *public-relations counselor*, William M Dobson, Northampton

MIDDLESEX EAST — *President*, Justin L Anderson, Reading, *vice-president*, Walter H Flanders, Melrose, *secretary*, Roy W Layton, Melrose, *treasurer*, Albert E Small, Melrose, *executive counselor*, Edward M Halligan, Reading, *legislative counselor*, John M Wilcox, Woburn, *public-relations counselor*, Milton J Quinn, Winchester

MIDDLESEX NORTH — *President*, Adam E Shaw, Lowell, *vice-president*, William F Ryan, Lowell, *secretary*, Brendan D Leahy, Lowell, *treasurer*, Mason D Bryant, Lowell, *executive counselor*, William F Ryan, Lowell, *legislative counselor*, Archibald R Gardner, Lowell, *public-relations counselor*, Daniel J Ellison, Lowell

MIDDLESEX SOUTH — *President*, Harold G Giddings, Newton Centre, *vice-president*, John F Case, Allston, *secretary*, Alexander A Levi, Newton Centre, *treasurer*, Fabian Packard, Belmont, *orator*, Robert E Gross, Framingham, *executive counselor*, Harold G Giddings, Newton Centre, *legislative counselor*, Edward J O'Brien, Jr, Brighton, *public-relations counselor*, Gordon M Morrison, Waban

NORFOLK — *President*, Dean S Luce, Canton, *vice-president*, John H Cauley, Dorchester, *secretary*, Basil E Barton, West Roxbury, *treasurer*, Frederick Reis, Jamaica Plain, *executive counselor*, Charles J Kickham, Brookline, *legislative counselor*, Humphrey L McCarthy, West Roxbury, *public-relations counselor*, Norman A Welch, West Roxbury

BERKSHIRE

P J Sullivan, Dalton, *supervisor*
 I S F Dodd, Pittsfield
 A C England, Pittsfield
 M M Brown, North Adams
 W T Frawley, Pittsfield

BRISTOL NORTH

W H Allen, Mansfield, *supervisor*
 J L Murphy, Taunton
 A J Leddy, Taunton
 L E Butler, Taunton
 J H Brewster, Attleboro

BRISTOL SOUTH

Henry Wardle, Fall River, *supervisor*
 E A McCarthy, Fall River
 F M Howes, New Bedford
 W F MacKnight, Fall River
 C C Persons, New Bedford

ESSEX NORTH

R V Baketel, Methuen, *supervisor*
 L C Peirce, Newburyport
 P W Blake, Andover
 C H Birdsall, Haverhill
 C R Hines, Amesbury

ESSEX SOUTH

A E Parkhurst, Beverly, *supervisor*
 J C Adams, Salem
 R A Harpin, Lynn
 I B Hull, Gloucester
 W C Inman, Danvers

FRANKLIN

J E Moran, Greenfield, *supervisor*
 P N Freeman, Greenfield
 H R Mahar, Orange
 F W Dean, Northfield
 C R Vinal, Turners Falls

HAMPDEN

Frederic Hagler, Springfield, *supervisor*
 A F G Edgelow, Springfield
 J M Gilchrist, Springfield
 G D Henderson, Holyoke
 John Pallo, Westfield

HAMPSHIRE

L B Pond, Easthampton, *supervisor*
 M E Cooney, Northampton
 T F Corriden, Northampton
 J E Hayes, Northampton
 C H Wheeler, Haydenville

MIDDLESEX EAST

M J Quinn, Winchester, *supervisor*
 J H Fay, Melrose
 C E Montague, Wakefield
 S H Moses, Winchester
 C R Baisley, Reading

MIDDLESEX NORTH

W F Ryan, Lowell, *supervisor*
 F R Brady, Lowell
 R C Stewart, Lowell
 H L Leland, Lowell
 J D Sweeney, Lowell

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 H Allan Novack, Brookline
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 R F Ross, South Braintree
 R R Ryan, South Weymouth
 W L Sargent, Quincy

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E L Perry, Middleboro, *supervisor*
 D W Pope, Brockton
 J H Dunn, Rockland
 J A Pettey, Brockton
 R E Swenson, Plymouth

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 H T Hutchins, Boston
 A J A Campbell, Boston
 W E Browne, Boston
 E F Timmins, South Boston

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 H K Spangler, Worcester
 George Ballantyne, Worcester
 E J Crane, Holden
 W E Murphy, Worcester

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 F J Djerf, Fitchburg
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ESSEX NORTH — F W Anthony, Haverhill
ESSEX SOUTH — O C Blair, Lynn
FRANKLIN — K W D Jacobus, Turners Falls
HAMPDEN — F K Dutton, Springfield
HAMPSHIRE — W M Dobson, Northampton
MIDDLESEX EAST — I W Richardson, Wakefield
MIDDLESEX NORTH — J F Boyle, Lowell
MIDDLESEX SOUTH — H P Stevens, Cambridge
NORFOLK — W J Walton, Dorchester
NORFOLK SOUTH — F A Bartlett, Wollaston
PLYMOUTH — J A Carnuolo, Brockton
SUFFOLK — J R Torbert, Boston
WORCESTER — W P Bowers, Clinton
WORCESTER NORTH — A P Lachance, Gardner

OFFICERS OF THE SECTIONS FOR 1946

ELECTED BY THE SECTIONS

SECTION OF MEDICINE

Chairman, Albert A Hornor, Boston, *vice-chairman*, Daniel J Ellison, Lowell, *secretary*, Francis C Hall, Boston

SECTION OF SURGERY

Chairman, Charles F Twomey, East Lynn, *secretary*, Alexander J A Campbell, Boston
Executive Committee — Stanley J G Nowak, Belmont and Boston (1 year), Edward L Young, Jr, Brookline and Boston (2 years), E Parker Hayden, Brookline and Boston (3 years)

SECTION OF PEDIATRICS

Chairman, Floyd R Smith, Pittsfield, *secretary*, Gerald N Hoeffel, Cambridge
Executive Committee — Chairman, Philip H Sylvester, Boston, James Marvin Baty, Belmont and Brookline, Leroy T Stokes, Haverhill

SECTION OF OBSTETRICS AND GYNECOLOGY

Chairman, Arthur F G Edgelow, Springfield, *vice-chairman*, William J McDonald, Boston, *secretary*, George Van S Smith, Brookline

SECTION OF RADIOLOGY

Chairman, George Levene, Chestnut Hill and Boston, *secretary*, Edward B D Neuhauser, Cambridge and Boston

SECTION OF PHYSIOTHERAPY

Chairman, Arthur L Watkins, Arlington and Boston, *secretary*, Howard Moore, Newton and Boston

SECTION OF DERMATOLOGY AND SYPHILOLOGY

Chairman, Bernard Appel, Lynn, *secretary*, Fenner A Chace, Fall River

SECTION OF ANESTHESIOLOGY

Chairman, Sidney C Wiggins, Waban and Jamaica Plain, *secretary*, Leo V Hand, Newton Highlands and Boston

BERKSHIRE — *President*, Thomas H Nelligan, Pittsfield, *vice-president*, N Newall Copeland, Pittsfield, *secretary*, Daniel N Beers, Pittsfield, *treasurer*, Theodore W Jones, Pittsfield, *executive councilor*, Isaac S F Dodd, Pittsfield, *legislative councilor*, Clement F Kernan, Pittsfield, *public-relations councilor*, Patrick J Sullivan, Dalton

BRISTOL NORTH — *President*, William M Stobbs, Attleboro, *vice-president*, Joseph V Chatigny, Taunton, *secretary*, William J Morse, Attleboro, *treasurer*, Charles E Hoyer, Taunton, *executive councilor*, William H Allen, Mansfield, *legislative councilor*, Ralph M Chambers, Taunton, *public-relations councilor*, James H Brewster, Attleboro

BRISTOL SOUTH — *President*, John C Corrigan, Fall River, *vice-president*, S Perry Wilde New Bedford, *secretary and treasurer*, James E Fell, Fall River, *executive councilor*, Edwin D Gardner, New Bedford

ESSEX NORTH — *President*, Percy J Look, Andover, *vice-president*, Guy L Richardson, Haverhill, *secretary*, Harold R Kurth, Methuen, *treasurer*, Lawrence Murphy, Newburyport, *executive councilor*, Frank W Snow, Newburyport, *legislative councilor*, Edward H Ganley, Methuen, *public-relations councilor*, Harold R Kurth, Methuen

ESSEX SOUTH — *President*, William R Irving, Gloucester, *vice-president*, John W Trask, Lynn, *secretary*, Henry D Stebbins, Marblehead, *treasurer*, Charles F Deering, Danvers, *executive councilor*, Walter G Phippen, Salem, *legislative councilor*, Charles A. Worthen, Lynn, *public-relations councilor*, Loring Grimes, Lynn

FRANKLIN — *President*, Kenneth H Rice, South Deerfield, *vice-president*, John B Temple, Shelburne Falls, *secretary and treasurer*, Harry L Craft, Ashfield, *executive councilor*, William J Pelletier, Turners Falls, *legislative councilor*, Howard M Kemp Greenfield, *public-relations councilor*, John E Moran, Greenfield

HAMPDEN — *President*, Merrill F Hosmer, Springfield, *vice-president*, Patrick E Gear, Holyoke, *secretary and treasurer*, George C Steele, West Springfield, *executive councilor*, William A R Chapin Springfield, *legislative councilor*, Arthur Riordan, Indian Orchard, *public-relations councilor*, Patrick E Gear, Holyoke

HAMPSHIRE — *President*, Arthur N Ball Northampton, *vice-president*, Elmer H Copeland Northampton, *secretary and treasurer*, Mary P Snook, Worthington, *librarian*, Abbie M O'Keefe, Northampton, *executive councilor*, Joseph D Collins, Northampton, *legislative councilor*, Arthur N Ball, Northampton, *public-relations councilor*, William M Dobson, Northampton

MIDDLESEX EAST — *President*, Justin L Anderson Reading, *vice-president*, Walter H Flanders, Melrose, *secretary*, Roy W Lavton Melrose, *treasurer*, Albert E Small, Melrose, *executive councilor*, Edward M Halligan, Reading, *legislative councilor*, John M Wilcox, Woburn, *public-relations councilor*, Milton J Quinn, Winchester

MIDDLESEX NORTH — *President*, Adam E Shaw, Lowell, *vice-president*, William F Ryan, Lowell, *secretary*, Brendan D Leahan, Lowell, *treasurer*, Mason D Bryant, Lowell, *executive councilor*, William F Ryan, Lowell, *legislative councilor*, Archibald R Gardner, Lowell, *public-relations councilor*, Daniel J Ellison, Lowell

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NORFOLK — *President*, Dean S Luce, Canton, *vice-president*, John H Cauley, Dorchester, *secretary*, Basil E Barton, West Roxbury, *treasurer*, Frederick Reis, Jamaica Plain, *executive councilor*, Charles J Kickham, Brookline, *legislative councilor*, Humphrey L. McCarthy, West Roxbury, *public-relations councilor*, Norman A Welch, West Roxbury

OFFICERS OF THE DISTRICT MEDICAL SOCIETIES FOR 1945-1946

BARNSTABLE — *President*, Joseph N Kelly, Orleans, *vice-president*, Harold F Rowley, Harwich Port, *secretary*, Julius G Kelley, Pocasset, *treasurer*, Frank Travers, Barnstable, *librarian*, Carroll H Keene, Chatham, *executive councilor*, Paul M. Butterfield, Harwich, *legislative councilor*, Julius G Kelley, Pocasset, *public-relations councilor*, William D Kinney, Harwich

NORFOLK SOUTH — *President*, Frank W. Crawford, Holbrook, *vice-president*, David L. Belding, Hingham, *secretary*, Ebenezer K. Jenkins, Braintree, *treasurer*, Francis G. King, Quincy, *executive councilor*, Daniel B. Reardon, Quincy, *legislative councilor*, David L. Belding, Hingham, *public-relations councilor*, Nahum R. Pillsbury, Braintree

PLYMOUTH — *President*, Paul B. Kelly, Plymouth, *vice-president*, Walter H. Pulsifer, Whitman, *secretary*, Ralph C. McLeod, Brockton, *treasurer*, Rudolph A. Kruger, Brockton, *executive councilor*, Perce H. Leavitt, Brockton, *legislative councilor*, John J. McNamara, Brockton, *public-relations councilor*, Charles D. McCann, Brockton

SUFFOLK — *President*, Donald Munro, Boston, *vice-president*, Charles C. Lund, Boston, *secretary*, Robert L. Goodale, Boston, *treasurer*, Richard S. Eustis, Boston,

executive councilor, Alexander J. A. Campbell, Boston, *legislative councilor*, William E. Browne, Boston, *public-relations councilor*, Albert A. Hornor, Boston

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ADMISSIONS RECORDED FROM MAY 23, 1944, TO MAY 23, 1945

YEAR OF ADMISSION	NAME AND RESIDENCE	MEDICAL SCHOOL
1944	Anderson, Ruth Messer, West Roxbury	Boston University
1944	*Asaf, Boris George, Brockton	Middlesex
1945	Avery, Jean Copeland, Framingham	Boston University
1944	Bagnall, Richard Salmon, Groveland	Harvard
1944	Bandeian, Alice Mardros Kechijian, Westwood	Boston University
1945	Beckman, William Woods, Cambridge	Harvard
1944	Berenberg, William, Brookline	Boston University
1945	Bird, Kenneth Thomas, Waltham	Harvard
1944	*Bloomenthal, Herbert Myer, Allston	Middlesex
1945	Bloomfield, Richard Adolph, Boston	Harvard
1945	Boehme, Earl James, Chestnut Hill	University of Minnesota
1944	*Bowman, Rose Marie, North Adams	Middlesex
1944	*Bowman, William Elderdice, North Adams	Middlesex
1944	Bradley, Stanley Edward, Boston	University of Maryland
1945	Branca, Alfred William, Dorchester	Tufts
1944	Bromwell, Chester Edward, Boston	Boston University
1944	*†Brown, Sylvan George, Concord, N. H.	College of Physicians and Surgeons, Boston
1945	Bushueff, Boris Paul, Waltham	Harvard
1944	Cataldo, Robert Joseph, Waltham	Tufts
1944	Cherry, Harriet Elisabeth, Springfield	Tufts
1944	Chiampa, Francis Paul, Boston	Tufts
1945	*Colby, Fred Bennett, Fitchburg	University of Lausanne
1945	Cotton, Bert Hollis, Newton Centre	University of Oklahoma
1944	Crimmings, Francis John, Lovell Gen. Hosp.	Tufts
1945	Cyr, Donat Paul, Newton Centre	Georgetown University
1944	*Daiute, Eleanor Doris, South Braintree	Middlesex
1944	Davidson, Charles Sprecher, Boston	McGill University
1944	*Davis, Paul, Boston	Kansas City University of Physicians and Surgeons
1944	*Dorne, Raymond M., Quincy	Middlesex
1944	Dutra, Frank Robert, Boston	Northwestern University
1945	*Edelman, Waldo George Albert, Agawam	College of Physicians and Surgeons, Boston
1945	*Eidam, Carl Louis, Lawrence	Royal College of Physicians and Surgeons, Edinburgh, Scotland
1944	*Farley, Edward John, Stoughton	Middlesex
1944	Favour, Cutting Broad, Boston	Johns Hopkins
1944	Ferrebee, Joseph Wiley, Boston	Harvard
1944	Fitzgerald, Patrick James, Boston	Tufts
1943	Gigger, Augustus George, Woods Hole	Boston University
1944	*Goldberg, Bernard, Allston	Friedrich-Wilhelms University
1944	Goodof, Irving Israel, Newtonville	Boston University
1945	Gorman, John Joseph, Fall River	College of Physicians and Surgeons, Baltimore
1944	*Grant, Maurice David, North Attleboro	Middlesex
1945	*Greenfield, Harold Beryl, Winthrop	College of Physicians and Surgeons, Boston
1945	Grice, David Stephen, Cambridge	University of Rochester
1945	Hays, Robert Augustine, Waltham	Tufts
1944	Hendrick, Ives, Belmont	Yale University
1945	Heusner, Albert Price, Boston	Harvard
1944	*Higgins, Clarence Bertrand, Milton	Middlesex
1944	Hoffman, Howard Allen, Brookline	New York Medical College
1945	Howes, Hermon E., South Chatham	Boston University
1944	Illingworth, Myles Henry, Boston	Tufts
1944	James, Harriet Dorothy, Brookline	University of Minnesota
1944	Jones, Stewart Hayner, Brookline	McGill University
1944	Joslin, Eric F., West Stockbridge	Albany Medical College

*The candidate after a personal interview was approved by the Committee on Membership and permitted to take an examination before a board of censors

†Admitted to non resident fellowship

YEAR OF ADMISSION	NAME AND RESIDENCE	MEDICAL SCHOOL
1944	Kane, Lewis Williams, Charles River Village	Harvard
1945	*Katelyan, Abraham Eugene, Brighton	Middlesex
1944	Kreidberg, Marshall Bradford, Dorchester	Tufts
1945	Kressler, Augusta Holmstock, Worcester	Women's Medical College of Pennsylvania
1944	*Kurtzmann, Rudolf, Norfolk	University of Vienna
1945	Kuntz, Harriette H., Dennis	Northwestern
1944	Landngan, Frederick Laurence, West Roxbury	Tufts
1944	Landry, Christopher Lee, Boston	Tufts
1944	*Langer, Edward Maurice, West Springfield	Royal College of Physicians and Surgeons, Edinburgh, Scotland
1944	Leary, Theodore Moreau, Boston	George Washington University
1945	LeCompte, Philip Medford, Brookline	Yale
1944	Levin, Sidney, Brookline	Tufts
1944	Levine, Samuel, Camp Edwards	University of Michigan
1944	†Lindberg, Cosa Dell Haskell, Phoenix, Arizona	Boston University
1944	Linthwaite, Robert Frederick, Melrose	College of Medical Evangelists
1944	Lipsher, Leo, Roxbury	Tufts
1944	Lo-Presti, Joseph, Lawrence	New York University
1945	Logler, Frank Joseph, Beverly	Vanderbilt University
1945	Loud, Norman Wiley, Fall River	Harvard
1945	Mahoney, Hugh Francis, Tewksbury	George Washington University
1945	Mailey, Howard Douglas, Boston	Boston University
1944	Marcotte, Reo J., Pittsfield	University of Michigan
1945	*McCaffrey, Jerome Aloysius, Norton	Middlesex
1945	McKuttrick, John Byron, Brookline	Harvard
1944	McMackin, Francis Lillian, Boston	Boston University
1945	*Monyek, Milton Sonniel, West Springfield	Middlesex
1944	*Moore, Thomas James, Dorchester	Middlesex
1944	*Morelli, Dano, Wakefield	University of Naples
1944	Morrill, Donald Manly, Malden	University of Michigan
1945	Mostofi, Fathollah Keshvar, Boston	Harvard
1945	Moyer, John Henry, Worcester	University of Pennsylvania
1945	Neylan, Marguerite Mary, Boston	New York Medical College
1945	Orlov, Morton, Roxbury	Tufts
1945	Osborne, Joseph, Newton Center	Boston University
1945	Perry, Mary Elizabeth, West Somerville	Tufts
1945	Phillips, Joseph Henry, Brookline	Harvard
1945	*Posner, Sigmund Jacob, Ludlow	College of Physicians and Surgeons, Boston
1944	*Potash, Jacob, Lynnfield	Middlesex
1945	Pratt, Edward Lowell, Boston	Harvard
1944	Prout, Curtis, Chestnut Hill	Harvard
1945	Quinn, James Martin, New Bedford	Georgetown
1944	Richardson, George W., Everett	Tufts
1945	Robbins, Albert Ira, Roxbury	University of Vermont
1944	Robbins, Stanley Leonard, Brookline	Tufts
1944	Ross, Lawrence, Gloucester	Harvard
1944	*Rothmann, Eva, Boston	University of Berlin
1944	*Ryan, Thomas F., Housatonic	Middlesex
1945	Sagall, Elliot Lawrence, Boston	Harvard
1945	Scanto, Nina Edith, Methuen	Woman's Medical College of Pennsylvania
1945	Shannon, Martin Joseph, Jr., Lawrence	Tufts
1944	*Sirulnik, Frank, Springfield	Middlesex
1945	Smith, M. Frances Hayward, Boston	Boston University
1944	Smyth, Henry Field, Pocasset	University of Pennsylvania
1944	Stare, Fredrick John, Waban	University of Chicago
1944	*Steinhardt, Arthur Hermann, Springfield	University of Goettingen (Germany)
1944	Sterman, Ida Anne, Brookline	Boston University
1944	Sylvester, Rowland Emerson, Auburndale	Boston University
1945	Thompson, Kenneth Wade, Dedham	Harvard
1944	Traustein, Maurice, Jr., Winthrop	University of Vermont
1944	*Waitkus, Algird Augustine, Brockton	Middlesex
1945	Wanning, Patricia Emerson, Cambridge	Yale
1945	*Westlin, Richard Volmar, North Leominster	Imperial Alexanders University in Helsingfors (Finland)
1945	Wilson, James Cornelius, Edgartown	University of Vermont
1945	Wright, Richard Henry, Mattapan	Tufts
1944	Yahn, George Washington, III, Boston	University of Cincinnati
1945	Zeltzman, Morris, Walpole	Tufts
	Total	119

*The candidate after a personal interview was approved by the Committee on Membership and permitted to take an examination before a board of censors

†Admitted to non resident fellowship

DEATHS REPORTED FROM MAY 23, 1944, TO MAY 23, 1945

ADMITTED	NAME	PLACE OF DEATH	DATE OF DEATH	AGE
1885	†Allen, Gardner Weld	Boston	July 12, 1944	88
1915	Austin, James Cornelius	Spencer	July 10, 1944	68
1933	Barone, Anthony	Boston	December 8, 1944	48
1916	Battershall, Jesse Wolfenden	Attleboro	May 4, 1945	51

†Retired fellow

ADMITTED	NAME	PLACE OF DEATH	DATE OF DEATH	AGE
1913	Bauman, Julia Lewandowska	Holyoke	November 17, 1944	62
1902	Bennett, William Hurlburt	Norwell	March 5, 1945	76
1903	Bergin, Stephen Albert	Worcester	February 22, 1945	71
1921	Berman, Saul	Chestnut Hill	September 18, 1944	43
1921	Bishop, William Atkins	Watertown	February 14, 1945	56
1912	Blaisdell, John Harper	Boston	October 25, 1944	53
1912	†Blanchette, William Henry	Fall River	August 1, 1944	70
1911	Bonneville, Alfred Joseph	Northampton	January 11, 1945	73
1935	Bray, Thomas Ambrose	Holliston	April 1, 1945	50
1920	Breed, William Bradley	Boston	August 21, 1944	51
1931	Brown, Edison William	Revere	August 18, 1944	63
1895	†Bruce, Daniel Angus	Quincy	November 5, 1944	81
1874	†Bulfinch, George Greenleaf	Brookline	March 14, 1944	95
1892	†Butler, John Edward	Taunton	March 9, 1945	81
1908	Casselberry, Clarence Marmaduke	Newton	February 23, 1945	69
1940	Chesbro, Wallace Leo (Lt Cdr, MC, U S N R)	U S S Comfort, South Pacific	April 28, 1945	31
1908	Christiennin, Charles Leonard	Maplewood, N J	October 18, 1944	66
1892	†Cobb, Albert Crocker	Marion	March 21, 1945	76
1893	Cobb, Farrar	Hyannis	May 28, 1944	67
1925	Cook, Edward Moody	York Harbor, Me	May 20, 1944	45
1899 } 1907 }	Crawford, Francis Xavier	Dorchester	August 19, 1944	71
1904	Cummings, John Joseph	Worcester	July 9, 1944	74
1928	Curtin, John Joseph	Waltham	March 10, 1944	60
1934 } 1939 }	Dawson, Raymond John	Methuen	November 20, 1944	38
1894	†Dion, Thomas Joseph	Boston	November 27, 1944	76
1906	Downing, Andrew Francis	Cambridge	June 2, 1944	66
1887 } 1934 }	†Draper, Frank Eugene	Framingham	November 24, 1944	80
1900	†Duckering, William West	Dorchester	May 3, 1945	83
1921	Dudley, Oscar Albert	Shrewsbury	October 28, 1944	60
1936	Dunn, Raymond Anthony (Lt, JG, MC, U S N R)	At sea	Time of invasion of Sicily	33
1914	†Eliot, Henry Whitney	Manchester, Vt	October 21, 1944	78
1893	†Faulkner, Herbert Kimball	Keene, N H	September 15, 1944	85
1905	Fenwick, George Benson	Chelsea	October 27, 1944	67
1919	Fisher, John Charles Vincent	West Roxbury	February 20, 1945	52
1909	Flagg, Harry Howard	Charlestown	May 25, 1944	63
1915	Frasier, Joseph Anthony	New Bedford	May 20, 1945	69
1924	Gagnon, Alphonse Paul	Taunton	August 2, 1944	52
1919	Goddard, Frederick Chambers	Uxbridge	November 7, 1944	52
1910 } 1918 }	Gookin, Edward Richard	Washington, D C	March 7, 1945	63
1915	Greene, Jeremiah Augustine	Cambridge	April 6, 1945	59
1916	Halton, Edward Peter	Holyoke	October 18, 1944	62
1913	†Haslam, Frank Alden	Allston	December 31, 1944	82
1904	Haviland, Walter Childs	Mansfield Depot, Connecticut	May 14, 1945	63
1887	Hawes, Edward Everett	Hyannis	November 30, 1944	82
1940	Heavey, Thomas J	Medway	August 7, 1944	58
1917	Herbert, Edward	Fall River	June 26, 1944	69
1909 } 1943 }	Hirsch, Henry Leon	Springfield	May 8, 1945	60
1911	†Hopkins, William Thorpe	Lynn	April 10, 1945	76
1901	Johnson, David Joseph	Boston	October 7, 1944	71
1892	Jones, Lombard Carter	Falmouth	August 17, 1944	78
1892	Keleher, William Henry	Woburn	December 4, 1944	75
1928	Kelley, Harry Norton	Worcester	February 20, 1945	45
1924	Kickham, Edward Leonard	Brookline	August 10, 1944	48
1888	†King, Nathaniel Clark	Brookline	January 23, 1945	83
1892	†Knowlton, Charles Davison	Rockport	January 5, 1945	77
1911	Lawrence, Charles Henry	Brookline	March 13, 1945	62
1934	Lehnherr, Earl Rudolph	Brookline	December 4, 1944	41
1919	Leib, Edwin Roy	Worcester	May 3, 1945	70
1938	Levin, Harry Marvin (Surgeon, U S P H S (R))	U S S Serpens at Guadalcanal	January 29, 1945	41
1914	MacDonald, Frederick Livingstone	Waltham	May 24, 1944	65
1917	†Mahoney, John Lewis	St Petersburg, Florida	January 2, 1945	72
1931	Makler, Mark Irving	Lynn	May 14, 1945	42
1923	Marshall, John Ross (Cdr, MC, U S N R)	Shoemaker, California	October 14, 1944	56
1891	†McCarthy, Eugene Allan	Concord	January 1, 1945	84
1918	†Moir, Marguerite Winifred	Boston	December 3, 1944	71
1898 } 1911 }	†Moody, Flora Frost	Springfield	June 26, 1944	73
1898	Moore, John Henry	Boston	Unknown (Around Feb '45)	Unknown
1892 } 1928 }	Morse, Frank Leander	Somerville	November 5, 1944	73
1890	†Noyes, Nathaniel Kingsbury	Plymouth	April 12, 1945	89
1904	• Ober Ralph Beverly •	Sarasota, Fla	April 13 1945	65
1897	†O'Neil, Richard Frothingham	Boston	November 30, 1944	70

ADMITTED	NAME	PLACE OF DEATH	DATE OF DEATH	AGE
1933	Ossen, Emil Zola	Quincy	December 16, 1944	38
1921	†Outhouse, John Stanley	Shelburne Falls	June 20, 1944	69
1914	Perkins, Roy Stanley	Ayer	December 3, 1944	54
1916	Porter, Charles Terrell	Boston	April 19, 1945	56
1916	Reeves, Marcellus	Boston	October 15, 1944	81
1907 } 1925 } 1935 }	Richardson, Cheslie Alvah Clarence	Somerville	January 30, 1945	Unknown
1925	Rudy, Abraham	Brookline	February 19, 1945	49
1909	Sanborn, Byron	Topsfield	December 20, 1944	70
1935	Sanderson, Robert (Lt., MC, U S N R.)	Arlington, Va (In service of his country)	February 21, 1945	41
1916	Scanto, Nicholas Julius	Methuen	December 3, 1944	65
1921	Shaughnessy, Michael James	Framingham	February 17, 1945	63
1893	†Shaw, Albert Joel	Newton	May 23, 1944	72
1930	Sheedy, John Francis	Lawrence	Unknown (Around April '45)	73
1882	†Sherman, Frank Morton	West Newton	September 14, 1944	87
1903	Sims, Frederick Robertson	Sandwich	October 26, 1944	65
1816	Siskind, Alexander Louis	Boston	May 5, 1944	77
1914	Sparks, Ernest Elliot	Cochituate	July 21, 1944	71
1910	Sparrow, Charles Atsatt	Worcester	September 20, 1944	60
1891	Thompson, Charles Oscar	Boston	January 29, 1945	82
1917	Trask, Harry Wallis	West Boylston	November 4, 1944	63
1895	†Varney, Fred Elbridge	North Chelmsford	June 7, 1944	83
1929	Watson, Lester Dow (U S P H S)	Long Island, N Y (In the Service)	June 14, 1944	43
1928	†Whitmarsh, Willard Francis	Bridgewater	May 15, 1944	79
1903 } 1925 }	Wiggin, William Irving	Lowell	January 3, 1945	65
1945	Young, Edward Lorraine III (Capt., MC, A U S)	In action in Germany	March 24, 1945	30

†Retired fellow

Total number of deaths of active fellows	74
Total number of deaths of retired fellows	26
Grand total	100

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 31301

PRESENTATION OF CASE

First admission. A sixty-five-year-old police chief was admitted to the hospital because of jaundice, chills, malaise, nausea and vomiting.

The patient had always been well and active until about five months before entry, when his urine became dark, one week later the scleras and face became slightly yellow. He continued to feel well and worked until about three weeks after the onset of jaundice, when one day he had a chill, slight fever, malaise and that night was nauseated and vomited. There was no pain. Soon after that episode he became markedly jaundiced. He was admitted to a community hospital for a period of two weeks, during which time the urine remained dark, the stool became clay-colored and the deep jaundice persisted. The patient left the hospital on a fat-free diet, feeling much better, the stools were yellow, but the jaundice remained and pruritus became marked. At home he remained quite well and without much change until one month before admission, when fairly severe malaise reappeared, which persisted until five days before admission. Two weeks before admission he began to have a "dull soreness" in the right upper quadrant, this extended to the left upper quadrant and was associated with transient sharp shooting pain in the same region and also in the region of the left scapula. These pains were almost constant during the two weeks before admission and were severest after meals. During the month before admission the jaundice gradually became less intense and the urine became lighter in color, the stools at the time of admission were of normal color. During this five-month illness his weight had fallen from 235 to 186 pounds. He had no awareness of food intolerances. He never drank alcoholic beverages.

The patient's father, one of six sisters and one of two sons had died of tuberculosis.

Physical examination revealed a markedly jaundiced, well developed man showing evidence of recent weight loss. The heart and lungs were normal. The abdomen was flat and soft. The right lobe of the liver was palpable three fingerbreadths

below the costal margin and presented a smooth even edge. The upper border was percussed at a normal level. The left lobe was apparently not enlarged by percussion posteriorly. In the mid-epigastrium, extending from the tip of the xiphoid halfway to the umbilicus was a round firm nontender mass about 5 cm in diameter. It descended with inspiration and was indistinguishable from the liver.

The temperature, pulse and respirations were normal. The blood pressure was 130 systolic, 68 diastolic.

Examination of the blood showed a white-cell count of 6400, with 64 per cent. neutrophils, and 10.5 gm of hemoglobin. The urine was light amber and contained no bile, the sediment showed 15 red cells and a rare white cell per high-power field. Several stools were brown and guaiac negative. The blood Hinton test was negative. The serum non-protein nitrogen and protein were normal. A van den Bergh showed 2.9 mg of bilirubin direct and 3.3 mg indirect. The prothrombin time was 21 seconds (normal, 18 to 20 seconds). A bromsulfalein test was normal.

By x-ray examination the liver and spleen were thought to be of normal size. No unusual areas of calcification were seen. A Graham test did not outline the gall bladder. On the third day a peritoneoscopy showed that the left lobe of the liver and the region of the mass were concealed by adhesions of the omentum to the anterior abdominal wall that obliterated almost the entire left upper quadrant. The right lobe of the liver was readily seen. The edge appeared rounded and smooth, it was grayish, with a slightly thickened capsule. No nodular areas were seen. There was no fluid, and the serosa was smooth. A gastrointestinal series showed a normal esophagus. In the fundus of the stomach, extending from the cardia upward and lying somewhat anteriorly, there was a defect by what appeared to be a large soft-tissue mass (Fig 1). The mucosal pattern was not definitely traceable through this region. The edges of the defect were quite sharp. A seemingly distinct and definitely extrinsic mass was seen pressing on the lesser curvature of the stomach somewhat anteriorly. This represented the mass palpable in the abdomen. Barium passed through the pylorus without hesitation and filled the duodenal bulb. The duodenal loop appeared smaller than usual, and the mucosal pattern was everywhere normal.

The patient was given a transfusion, and on the tenth day an exploratory laparotomy was performed. The omentum was found to be densely adherent to the anterior surface of the liver. The tumor could be palpated and was believed to lie in the stomach, although the latter was not visualized in the region of the tumor. An opening was made through the gastrocolic omentum, and the posterior surface of the stomach was explored. No

*On leave of absence.

adhesions were found there. The mass was then investigated, and on attempting to dissect away the omentum, a large subdiaphragmatic abscess was found. An extensive prophylactic drainage was deemed necessary and was performed. A culture of the abscess showed a moderate number of colonies of nonhemolytic streptococci and a few of colon bacilli. The prothrombin time was 30 seconds and over a two-week period fell gradually to 22 seconds. The van den Bergh test became too low to read. Cephalin flocculation tests were +++ to +++++, and a bromsulfalein test showed 30 per cent reten-

On physical examination he was found to be jaundiced. The sinus was draining a moderate amount of reddish-brown pus. The left lower chest was dull and showed diminished breath sounds and tactile fremitus. A friction rub was heard in the left chest anteriorly. The abdomen was soft, the liver and spleen were not felt. The epigastric mass appeared to be the same as on the first admission.

The temperature, pulse, and respirations were normal.

The urine was normal. The white-cell count was 11,200, with 62 per cent neutrophils, and the



FIGURE 1

tion thirty minutes after 2 mg of dye per kilogram of body weight had been injected.

The patient remained asymptomatic, with a good appetite, and only the drain in the left gutter continued to discharge. He was discharged to his home on the twenty-ninth postoperative day, with arrangements to return in three weeks for removal of the gastric lesion.

Second admission (one month later). During the interim the patient had been well, his appetite was good, he slept well, and there was no recognized recurrence of the jaundice. Two days before admission he had an episode of nausea and vomiting followed by a day of anorexia.

hemoglobin 10.7 gm. A repeat Hinton test was negative. A bromsulfalein test now showed 15 per cent retention in thirty minutes, and a van den Bergh test was 1.3 mg direct and 1.9 mg indirect. The prothrombin time was normal. X-ray examination of the chest showed a moderate amount of fluid in the left pleural cavity. The lung fields were clear. The heart and mediastinum were not displaced. The heart and right diaphragm were normal. The left half of the diaphragm was obscured by fluid and showed limited excursion. A plain film of the abdomen showed no enlargement of the liver. The spleen was not seen. The defect in the air-filled cardiac portion of the stomach was sepa-

rated from the diaphragm by approximately 5.5 cm. No gall-bladder calculi were seen. A gastrointestinal series was not significantly different from the former one. The patient was discharged on the third day.

Third admission (five weeks later) Following discharge he had felt well and strong. Two and a half weeks before admission he ate a fatty meal, which was followed by an episode of nausea and vomiting. There had been no weight loss.

Physical examination revealed the jaundice to be somewhat improved although still present. The liver was a little larger than previously, but the epigastric mass appeared unchanged. There were a few moist rales at the left base posteriorly, as well as a small area of dullness. The sinus was still draining.

The temperature, pulse, respirations and blood pressure were normal.

The urine was normal except for the presence of urobilinogen in a dilution of 1:50. The white-cell count was 7600, with 72 per cent neutrophils, and the hemoglobin 10.9 gm. A stool was normal. The prothrombin time was 23 seconds. A gastrointestinal series suggested that the mass in the fundus of the stomach was somewhat smaller than at the last examination. Some fluid remained in the left costophrenic sinus, but the amount had markedly diminished.

The patient was given two whole-blood transfusions, and on the sixth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR ROBERT R. LINTON This case is puzzling to me. There is no question that this man had an upper abdominal lesion and it is up to me to try to make a diagnosis. As one reads the record it is obvious that the patient had a subdiaphragmatic abscess on the left side. It is important to note that he had been sick for a considerable period — four or five months. The presenting symptom when he first came in, in addition to general malaise, nausea, chills and vomiting, was jaundice of several months' duration. The striking thing about the jaundice is that it was of an intermittent type, despite the fact that nothing was done to the biliary system to try to relieve it. I am a little disappointed that in the operative note no mention is made of the gall bladder. I presume that it was not seen because it was involved in the inflammatory mass.

DR BENJAMIN CASTLEMAN Dr Sweet, can you answer that?

DR RICHARD H. SWEET We thought about the gall bladder but my attention was centered on the two masses — the one high in the fundus of the stomach and the one that turned out to be a subdiaphragmatic abscess. I palpated the gastric mass first and formed some judgment about that. Then I explored the midepigastric mass and immediately broke into pus. I made no effort to see the gall bladder.

DR CHESTER M. JONES The mass that you broke into was a tremendous one?

DR SWEET Yes — a huge abscess.

DR LINTON The laboratory studies do not help at all in the diagnosis.

There is a family history of tuberculosis, but I do not believe that his condition was due to an acid fast infection.

It is rather surprising, in view of the subphrenic abscess, that this man did not have more fever. The temperature was normal throughout the course in the hospital. Furthermore, he had no leukocytic response to the abscess.

DR JONES Those things bothered us, too.

DR LINTON One of the conditions that I have to consider is pancreatitis. That seems unlikely in view of the fact that the lesser peritoneal cavity did not appear to be involved by the inflammatory mass at the time of exploration, as I understand it. Since the pancreas lies in the lesser peritoneal cavity, I should think that, if he had had a pancreatitis, it would have been obvious.

I should like to see the x-ray films.

DR GEORGE W. HOLMES The upper film shows the stomach fairly well, and it is obvious that there is a large pressure defect on the lesser curvature and another in the region of the fundus. It would be helpful if I could say whether the stomach was actually involved, that is, whether the ulcer crater went out into this area, but I cannot. From the reports, the man who did the examination thought that there was actual involvement of the stomach. Of course, in a picture like this, one thinks of sarcoma, but we have insufficient proof to make such a diagnosis. An attempt was made to show the gall bladder, but apparently it did not fill with the dye.

DR LINTON They did a gastrointestinal series later. Are those films here?

DR HOLMES Yes, but so far as the stomach is concerned there has not been any great change. There is something here that might be said to be a mass inside the stomach, which was not there before. I should like to know whether it was food or whether it was a mass. It could be either. If it was a mass, it means that whatever it was had extended into the stomach.

The chest may be of some interest. I should say that it was quite normal. It certainly does not show anything except a high diaphragm on the left.

DR LINTON I believe that the findings in the chest, as reported in the history, indicate an inflammatory process in the upper abdomen. I do not believe that he had a primary condition within the chest, and anything seen by x-ray is probably secondary to the subphrenic abscess. Is it possible that this man had a liver abscess, which could explain the jaundice and also, possibly, the subphrenic abscess? It seems unlikely because I do not believe

at a patient with a liver abscess would run a normal temperature and have a normal white-cell count. I so think that it would be unusual to have an intermittent type of jaundice, unless the liver abscess self were drained.

It seems to me that we are probably dealing with primary lesion in the stomach that had perforated into the upper abdominal cavity and had formed an abscess. The cultures are slightly in favor of an intestinal lesion that had perforated in view of the fact that they contained not only nonhemolytic streptococci but also colon bacilli.

Is it possible that this man had a perforated gastric ulcer? That seems quite unlikely in view of the fact that no lesion of that nature was seen by x-ray.

Another possibility, of course, is that this man had carcinoma of the stomach, with metastases beneath the diaphragm. There are some lymph nodes in that region, which, if enlarged, might have pressed down on the stomach. There is a possibility of lymphoma, but I do not know any way of making that diagnosis.

In summary, I favor an upper gastric lesion, probably a malignant tumor. This had perforated, and the abscess was drained, later an operation was done in an attempt to remove the lesion.

DR CASTLEMAN: How do you account for the jaundice?

DR LINTON: The only way that I can account for it is that the inflammatory mass must have produced pressure on the biliary system, which caused jaundice, when the inflammatory mass was drained, this relieved the pressure on the common duct.

DR CASTLEMAN: Dr Jones, will you give a brief summary of your observations on this man?

DR JONES: I saw this patient when he first came in. He was definitely jaundiced and had a tremendous nontender mass in the midepigastrium. With the story of the jaundice I thought, and subsequently Dr Sweet agreed, that the most reasonable diagnosis was malignant disease, with metastases to the liver that caused pressure on the bile duct. As we studied him, however, many queer things came to light that warranted exploration. The x-ray studies were quite striking. The pressure on the lesser curvature was obviously produced by the palpable mass. Then the finding of something additional in the stomach bothered us a great deal. Another thing that bothered us was the complete absence of fever and leukocytosis. It was striking that he continued to run an afebrile course, and so far as we could tell he had not had a fever before he came into the hospital. He was explored in the hope that we might find a situation that we could remedy, but with the thought that malignancy might be encountered.

At the first operation a subdiaphragmatic abscess was found, which explained the pressure on the lesser curvature of the stomach, and at the same

time Dr Sweet was able to palpate the stomach. That was as far as we were able to go. We thought, therefore, that we should give the patient a chance to recover from the first operation and then go in a second time for further examination of the stomach. We went over the x-ray films many times and wondered whether a leiomyosarcoma of the stomach was the explanation for the gastric mass. At the same time we were fairly sure that, since a subdiaphragmatic abscess had been found, it was not reasonable to assume that a gastric tumor was the cause. In other words, there might have been a primary cause for the jaundice and the subsequent subdiaphragmatic abscess. Even before the second operation we both decided that eventually the biliary tract had to be explored but that it could not be done at the second operation.

DR SWEET: As I have said, at the first operation I obtained an impression from feeling the gastric lesion, I thought that it was probably a leiomyosarcoma. It was a round hard mass which I could not see but could feel. The x-ray appearance also suggested that rather than carcinoma. The first operation was done with the thought that there might have been metastases to the liver, but none were found.

The second procedure was done through the chest, and I found a large hard round mass that was not easy to free because of the adhesions from the previous inflammatory process. It was obvious, ultimately, that this mass was not part of the stomach, it looked like spleen, although it had a peculiar shape. There was a normal-looking spleen, which I did not disturb. I took out the large mass.

CLINICAL DIAGNOSIS

Leiomyosarcoma of stomach?

DR LINTON'S DIAGNOSIS

Malignant tumor of stomach, with perforation

ANATOMICAL DIAGNOSES

Accessory spleen

Cholelithiasis

PATHOLOGICAL DISCUSSION

DR CASTLEMAN: I am afraid that we have made Dr Linton "the goat" for the sake of presenting an unusual condition. This peculiar mass proved to be an accessory spleen showing no abnormality microscopically. There was an acute perisplenitis and a subdiaphragmatic abscess.

DR LINTON: Is that not an unusual place for an accessory spleen?

DR CASTLEMAN: It is quite unusual, and it was the largest one that I have ever seen. It was not perfectly round. It had somewhat the shape of a normal spleen but did not have a hilus. The accessory spleen that one ordinarily sees is roughly 1 to

2 cm in diameter and perfectly round This one measured 12 by 7 by 5 cm

Will you tell us about the postoperative course, Dr Jones?

DR JONES We thought that we still had to go after the original cause and that the gastric lesion was a red herring, so to speak, being simply an interlude in a long story

In the next six months the patient gained a great deal of weight and was in relatively good condition He was jaundiced all the time, although at times clinical icterus was just barely present Repeated tests showed that he was having a gradual increase in hepatic involvement, in the sense that the dye retention slowly went up It is of interest that during this period the epigastric mass reappeared We attributed this to a gradual increase in the size of the left lobe of the liver to normal proportions, which it turned out to be at operation While he was being followed, the alkaline phosphatase rose steadily, reaching 30 Bodansky units per 100 cc, which practically always means biliary-tract obstruction, this is frequently due to a malignant tumor, although it can go as high as that with stone in the common duct The third operation was performed with the idea that the common duct and gall bladder should be explored, we thought that a stone would be found as the cause of the original jaundice and the other symptoms

DR SWEET At the final operation we explored the biliary tract, which was rather difficult of access because of the previous inflammatory process The common duct was immensely dilated, and on opening it I found a large stone lodged near the ampulla That was removed with ease, and no other stones were found The gall bladder was small, no longer than 2 cm, and had hardly any lumen At that time I saw no definite evidence of perforation, but I assumed that the abscess had resulted from a perforation of the gall bladder rather than from a perforation of the common duct

DR CASTLEMAN How did the liver look?

DR SWEET It was large and had a peculiar shape, the portion to the left of the ligament being much larger than that on the right, it was round and had a rather rough surface The spleen was palpated in its normal position

DR CASTLEMAN Biopsy of the liver showed an obstructive biliary cirrhosis

DR JONES There is one more point After the third operation the patient again became deeply jaundiced, but that subsequently receded, with gradual improvement in the bromsulphalein retention test Even now, however, two months later, the phosphatase has not returned to normal It takes many months for that to return to normal in cases of incipient biliary cirrhosis

DR WYMAN RICHARDSON Perhaps the white-cell count was normal because he had too much spleen How is that for a theory?

DR HOLMES We should have paid more attention to the fact that the Graham test did not visualize the gall bladder

CASE 31302

PRESENTATION OF CASE

A fifty-one-year-old brass grinder was admitted to the hospital because of dyspnea, cough and substernal pain

Five weeks before admission, on the way home from his laborious work, he developed a heavy feeling in his epigastrium that he thought was due to a cold For the first time he experienced shortness of breath, which progressed in severity despite constant bed rest The epigastric discomfort was not related to effort An irritating cough was at times productive of thick whitish sputum Associated with the epigastric discomfort, he also had an episode of chills, sweating and a fever up to 102°F, which lasted for five days Two and a half weeks before admission, there was a recurrence of chills and fever During the two weeks before entry he had episodes of severe nocturnal dyspnea, but with sedation and two to three pillows he slept well He had been allegedly digitalized before admission

Five years before admission he had passed a life insurance examination Two years before admission he had been treated for hypertension and headaches He had been a brass grinder for two years, working in poorly ventilated, dusty quarters

Physical examination revealed a well developed and nourished man in moderate respiratory distress, with fairly marked orthopnea The neck veins were slightly dilated when he lay flat Diffuse moist rales were heard throughout the chest, most marked at the left base The heart showed normal rhythm at a rate of 120 The point of maximal impulse was thought to be somewhat displaced to the left There was a coarse Grade-4 "wood-sawing" systolic murmur well transmitted to the back, as well as an early high-pitched diastolic murmur at the apex There was also a Grade-1 pulmonic systolic murmur with an accentuated second pulmonic sound, which was louder than the aortic second sound Pulsus alternans and an occasional third heart sound were detected Examination of the abdomen was negative The liver and spleen were not enlarged The extremities were slightly cyanotic

The temperature was 101.5°F, the pulse 120, and the respirations 30 The blood pressure was 130 systolic, 90 diastolic

Examination of the blood showed a red-cell count of 4,400,000, with 11.2 gm of hemoglobin, and a white-cell count of 6000, with 54 per cent neutrophils The urine had a specific gravity of 1.024 and was normal The serum nonprotein nitrogen was

mg per 100 cc., and the carbon dioxide 24.3 milliequiv per liter. An electrocardiogram showed sinus tachycardia at a rate of 125, a PR interval 0.16 second, a sagging ST₁, a slightly elevated S₁, a small S₂ and an inverted T₂ and T₃. There were prominent T waves in Leads CF₃, CF₄ and F₁, and sagging ST segments in Leads CF₄ and F₁. Q₁ measured 4 mm. By fluoroscopy the heart beat normally and both halves of the diaphragm showed limited motion.

An x-ray film of the chest showed the heart to be within normal limits, the cardiac-thoracic ratio being 13.5:29.0 cm. There was definite prominence of the left auricle, particularly posteriorly. There were flocculent areas of increased density scattered throughout both lung fields, more marked centrally and extending from the hilar shadows into the lung fields. There was no evidence of fluid on either side.

Repeated blood cultures showed no growth. The white-cell count rose to 11,000 on the fifth day and then remained unchanged. Throughout the patient's hospitalization the temperature was elevated to about 101°F every evening and returned to almost normal by morning. The pulse was erratic between 90 and 120. The respirations varied from 20 to 45. Fluid intake and output were low. He was maintained on digitalis and ammonium chloride. On the second day the blood pressure fell to 95 systolic, 60 diastolic, and remained at about that level until death. An x-ray film of the chest on the third day was unchanged. During the night and during periods when the heart rate was rapid, the sounds were poor and the patient became quite dyspneic. On the sixth day he coughed up bright-red rather frothy sputum, without chest pain of any sort. He remained dyspneic, and at that time high-pitched rales were heard at both bases and in the axillae. Another electrocardiogram on the sixth day showed no change. On the twelfth day he complained of some precordial pain. He was not orthopneic. He preferred to lie on his right side, with his head over the edge of the bed, and claimed that he felt better in that position.

On the thirteenth day the patient suddenly became critically ill, complaining of substernal distress. The blood pressure fell to 70 systolic, 50 diastolic, the pulse increased to 176 and was mildly irregular, and the respirations rose to 60. He was cyanotic, cold and clammy. The lungs filled with moist rales. After the administration of Cedilanid, aminophylline and oxygen and the application of tourniquets he improved, but the pulse and respiratory rates remained high. The chest pain became more pronounced, and the respirations became irregular and eventually ceased.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD O. WHEELER: This man died about seven weeks after the onset of an acute illness

characterized by chills, fever, shortness of breath and cough. Because of his occupation—he was a brass grinder—the question comes up whether this played any part in his illness. Did he have silicosis? He was working in poorly ventilated quarters exposed to dust. Two years is a relatively short period of exposure, but if he were working in a place where the concentration of silica in the dust was high, he might have developed this disease. Certainly the symptoms of shortness of breath and cough are consistent with silicosis. One does not see chills and fever, however, in uncomplicated silicosis. If he had a bronchopneumonia or tuberculosis along with the silicosis, he might have had chills and fever, and this would also explain the short duration of the illness. The loud systolic murmur and the symptoms of left ventricular failure are not, however, explained by this disease. Patients with a marked degree of silicosis occasionally develop chronic cor pulmonale, but this does not often occur. The electrocardiogram should help in making this diagnosis. As recorded in the protocol, the S₁ and Q₁ and the inverted T₂ and T₃ are slightly suggestive of right ventricular strain. Is the electrocardiogram here?

DR. BENJAMIN CASTLEMAN: You may see the one in the record.

DR. WHEELER: There is not much in this tracing to suggest right ventricular hypertrophy. There is no evidence of axis deviation, which is helpful because it tends to rule out aortic-valve disease and hypertensive disease, that is, conditions resulting in left ventricular hypertrophy. Because of the Q₁ and the inverted T₂ and T₃ he might have had a posterior myocardial infarct, but there is no change in the electrocardiogram taken six days later, furthermore, the absence of a Q₂ is against this diagnosis. I understand that the x-ray films are missing, which is unfortunate, for they might have helped a good deal in making the diagnosis.

DR. CASTLEMAN: Dr. Gardella, could you describe the films?

DR. J. WARREN GARDELLA: They are quite well described in the written report. There were flocculent areas radiating from the hilus of each lung.

DR. WHEELER: Did the X-ray Department think that this represented consolidation or pulmonary edema?

DR. GARDELLA: They were unable to say. The areas of flocculation were well defined and rather centrally located in both lung fields. The process was more marked on the right than on the left.

DR. WHEELER: The findings are suggestive of pulmonary edema, although the history is not that of a failing heart with pulmonary edema secondary to myocardial infarction.

DR. GARDELLA: I thought it significant that, despite the fact that he improved clinically so far as the heart and rales were concerned, the x-ray

picture remained the same. We then brought up the question of pneumoconiosis.

DR WHEELER The x-ray films were more suggestive of pulmonary edema than of pneumoconiosis, but I suppose that both might have been present.

To return to the findings in the heart, which are not explained by silicosis, it is said that he had a Grade-4 apical systolic murmur well transmitted to the back. That seems to indicate that he had mitral regurgitation. Aortic systolic murmurs are occasionally well heard at the apex but are not well transmitted to the back, as this murmur was.

It is interesting to note that five years before admission he passed a life-insurance examination, which suggests that the murmur was not present at that time. Two years later he was treated for hypertension. I do not know how to interpret the early high-pitched diastolic murmur at the apex, for the diastolic murmur due to mitral disease is low pitched rather than high and occurs in middiastole rather than in diastole. An aortic diastolic murmur might be transmitted to the apex, in which case it would be heard as an early high-pitched diastolic murmur, but usually such a murmur is better heard along the left sternal border. Then it is noted that the pulmonic second sound was increased, which, together with a pulsus alternans and gallop rhythm, indicates left ventricular failure, despite the fact that x-ray examination showed the heart to be normal in size. The x-ray films did show prominence of the left auricle, which is consistent with mitral disease.

In trying to tie in the cardiac findings with a febrile illness the first possibility that comes to mind is bacterial endocarditis, which can produce chills and fever and can cause death in a short time if congestive failure is present. An attractive possibility is that the patient developed subacute bacterial endocarditis on the basis of minimal rheumatic mitral disease, followed by rupture of a chorda tendinea, with the increased murmur and congestive failure. The difficulty in making that diagnosis is that the blood cultures were negative. Negative blood cultures, however, do not rule out subacute bacterial endocarditis.

I believe that hypertensive heart disease and chronic cor pulmonale are well ruled out. Could the patient have had a myocardial infarction five weeks before entry, which caused congestive failure and was associated with a pulmonary infection? That is a possibility. Such a condition might have caused left ventricular dilatation and a systolic murmur at the apex. Because of the electrocardiographic findings, however, it does not seem likely.

Then there are rare conditions that should be considered. This man might have had a virus infection with an associated myocarditis, but that is an unlikely possibility. There was no good evi-

dence of consolidation in the lungs, except for the fact that the pulmonary process did not clear up. On the other hand, pulmonary edema is frequently chronic and does not improve.

The best diagnosis I can make is subacute bacterial endocarditis superimposed on minimal rheumatic mitral disease, with an increase in mitral insufficiency, due to valve deformity or a ruptured chorda tendinea, leading to congestive failure and death.

CLINICAL DIAGNOSES

Coronary heart disease
Pulmonary edema
Pulmonary infarction?

DR WHEELER'S DIAGNOSES

Subacute bacterial endocarditis
Rheumatic heart disease, with mitral insufficiency
and possibly a ruptured chorda tendinea
Congestive failure, with pulmonary edema

ANATOMICAL DIAGNOSES

Coronary thrombosis, old and recent
Myocardial infarction of papillary muscle, healing, with deformity of mitral valve
Myocardial infarction, old posterior wall of left ventricle
Organizing pneumonitis, with extensive intra-alveolar fibrosis all lobes

PATHOLOGICAL DISCUSSION

DR CASTLEMAN The autopsy on this man showed a large heart, which weighed almost 500 gm. There was a bulge of the myocardium in the region of the posterior wall, which, when the heart was opened, proved to be a cardiac aneurysm (healed myocardial infarct). In places the wall was extremely thin, measuring only 2 mm. On the endocardial surface of this large, old infarct, which measured 6 by 4 cm, was an organized mural thrombus. The papillary muscle, which arises just above that point, was instead of the usual thick muscle bundle an extremely thin slightly fibrous band. This band had pulled away the posterior leaflet of the mitral valve so that when the valve closed it was incompetent. This thinning out of the papillary muscle was due to recent infarction at its base. So, although there was no bacterial endocarditis, the same principle was involved, that is, the infarct produced an effect that was tantamount to rupture of the muscle. The process was beginning to heal, and I believe that it was of about five weeks' duration. Rather far down in the right coronary artery there was an old thrombosis, which accounted for the healed infarct, as well as a more recent thrombus proximal to the old lesion. Perhaps the electrocardiogram did indicate posterior myocardial infarction.

he lungs were interesting, but I am not at all
an that I can fully explain the lesion. All five
s presented a similar appearance, being big
wet and weighing 2000 gm (normal, less than
1000 gm). On section the surfaces were gray and
nular. The process did not look like a true lobar
pneumonia or pulmonary edema but seemed to
be somewhere between the two. Microscopically
there were organizing fibrous tissue plugs in many
of the alveoli, alveolar ducts and respiratory
bronchioles. This picture was present in every lobe
of the lung. The only explanation I have for it is
that it represents an organizing unresolved pneu-
monia that began five weeks before entry, probably
the same time as the coronary thrombosis. There
are no fibrous plugs in the large bronchioles, so
that it cannot be called bronchiolitis fibrosa ob-
literans. In some alveoli we found fat-laden phago-
cytes and giant cells. There was no evidence, how-
ever, of tuberculosis or silicosis. This pulmonary
lesion reminds me of a case previously reported

here¹ in which there was a large thrombus in the
left auricle that obliterated the orifices of the pul-
monary veins of one lung, which showed a similar
alveolar fibrosis. It is quite possible that the in-
competence of the mitral valve, owing to the in-
farction of the papillary muscle, predisposed the
lung to develop this organizing process. This pic-
ture has been described by Masson² as a characteris-
tic feature in rheumatic pneumonia.

DR WHEELER: Rupture of a chorda tendinea
can occur spontaneously or with endocarditis, but
rupture of the papillary muscle almost always occurs
in infarct and leads to death within two or three
months, with congestive failure.

DR CASTLEMAN: This patient did not have com-
plete rupture.

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INCREASING AND MAINTAINING PENICILLIN BLOOD LEVELS

MANY methods have been recommended for delaying the absorption or the excretion of penicillin with the idea of maintaining high levels in the circulating blood for longer periods than are possible with simple injections of penicillin solutions. Such an effect is obviously desirable in certain subacute or chronic infections, such as syphilis, subacute bacterial endocarditis and osteomyelitis, that require treatment over long periods. Furthermore, the organisms in such cases often are not highly sensitive and, therefore, require greater concentrations than those that can be conveniently maintained by ordinary interrupted intramuscular

injections — and the use of continuous intravenous or intramuscular injections to accomplish this purpose is cumbersome and somewhat wasteful.

The methods for prolonging penicillin action have been reviewed and commented on recently in these columns.¹ Among those that seemed feasible and effective was the use of para-aminohippuric acid by constant intravenous infusion. This compound acts like Diodrast or other similar substances, apparently competing with the penicillin for excretion by the kidney tubules. Although para-aminohippuric acid is said to be nontoxic in the doses used and to be well tolerated for long periods, it has the undesirable features of any therapy that must be given by constant intravenous injection.

Bronfenbrenner and Favour² at the Peter Bent Brigham Hospital attempted to accomplish the same purpose with oral therapy. They utilized the principle involved in one of the well known liver function tests, namely, the conjugation of orally administered benzoic acid by the liver into hippuric acid and the excretion of the latter into the urine. Since the penicillin blocking power of benzoic acid was relatively small on an unrestricted diet, they combined a regime of fluid and salt restriction with the benzoic acid therapy. They also tried sodium benzoate but found that the added base tended to neutralize the effects of the controlled salt intake, and in addition, the dose of sodium benzoate given proved to be somewhat nauseating. On a normal diet 2.5 gm of benzoic acid was equivalent to 60 gm of sodium benzoate in raising penicillin levels.

The regime finally adopted consisted of keeping the daily caloric intake between 1500 and 2000 calories. The diet was otherwise restricted only by limiting the fluid intake to between 1000 and 1500 cc a day, and the salt to 3 gm or less a day. This gave a daily urinary output of 400 to 600 cc. The dose of benzoic acid was about 2.5 gm every four hours, either disguised by mixing it with food or given in four capsules of 0.6 gm each. Most patients preferred the latter. The benzoic acid was given twenty to thirty minutes before the intramuscular injection of penicillin. On the basis of observations in 6 patients these workers found that restriction of fluid intake to 1500 cc and of the salt intake to 3 gm a day doubles the penicillin blood level follow-

interrupted intramuscular injections of penicillin, the administration of benzoic acid to a patient on an unrestricted diet may double the usual penicillin blood level during similar treatment and that combination of these two procedures results in four-fold to eight-fold increase in penicillin blood level, with a prolonged effective blood concentration. This method is obviously simpler than its counterpart that requires constant intravenous injection of para-aminohippuric acid. Whether it will prove more useful than other methods, such as the intramuscular injection of penicillin in beeswax and peanut oil,³ remains to be seen. Both methods are worthy of clinical trial.

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HEALTH IN EUROPE

An attempt has been made in the March, 1945, issue of the *Statistical Bulletin* of the Metropolitan Life Insurance Company to evaluate the 1944 health conditions on the Continent. Various estimates of the European morbidity and mortality from causes other than violence have been put forward from time to time, but the figures are largely a matter of guesswork. Information on which the present study is based is fragmentary, being derived from several sources, chiefly the weekly epidemiological record of the Health Section of the League of Nations.

The situation in Germany showed signs of increasing deterioration, if the mortality from tuberculosis is assumed to be the best available index, there was an increase of about one third for the first quarter of 1944, compared with the first quarters of 1938 and 1939. Numerous cases of typhus fever occurred, cerebrospinal meningitis continued to be prevalent, and in the first nine months of the year about 200,000 cases of diphtheria were reported.

Typhus fever was also found to be prevalent in Holland, and in the liberated portion of Belgium the death rate was 22 per cent higher in October, 1944, than in the same month of 1943. Health conditions apparently remained fairly good in Den-

mark, although in both Denmark and France epidemic influenza was prevalent. The tuberculosis mortality in Paris showed a high level throughout the German occupation.

The record has been bad in Italy, even in the liberated portion, the death rate in Rome being reported as 17.7 per 1000, or more than 60 per cent above the 1940 rate. No figures are available for Poland, the unhappy country that has perhaps suffered more from foreign domination than has any in history. The incidence of typhus fever has remained high in the Balkan states. Tuberculosis is said by relief officials to have reached epidemic proportions in Greece, and in mid-1944 about 70 per cent of its population was reported to be suffering from malaria.

These estimates were collected and published prior to the collapse of Germany. Much more recently has come a report from Major General Warren Draper, deputy surgeon general of the United States Public Health Service and chief of the military government public-health branch of SHAEF in Paris, indicating that the health of both liberated countries and occupied Germany is not only "far better than generally supposed, but in many respects apparently approaching a normal peacetime standard." According to General Draper, however, the days ahead will be grim ones nutritionally for Europe, because of the disruption of normal supplies. One cannot help but wonder why, with the war over and millions of men released for productive labor, conditions should be so much worse for Europe generally than they were under nearly five years of German domination.

MASSACHUSETTS MEDICAL SOCIETY

PRESIDENT'S REPORT ON THE STATE OF THE SOCIETY*

ASSUMPTION and carrying of the leadership of this society bring a true comprehension of the potential activities and services that have not been initiated or developed. These war years have absorbed the available energies of every fellow of the Society. Nevertheless, I have been stimulated by the unselfish response of the busiest men in the

*An address delivered at the meeting of the Executive Committee of the Council of the Massachusetts Medical Society in lieu of the annual meeting of the Council, Boston, May 23, 1945.

Society to the invitation to service on committees Without this loyal support, the efforts of its leaders could accomplish little

The president of the Massachusetts Medical Society now spends about half his energy and time in performance of fundamental obligations of the office. The obligations of the office have priority over ordinary demands of practice. One of my friends said the other day that the Society ought to elect a retired fellow as president so as not to take the time of an active physician, but the job needs the energy and enthusiasm of a relatively young man, and he needs all the help that he can find.

I am sure there is, even now, latent energy that could be activated and used in the Society's service. If the district nominating committees were well chosen and better informed, and if they took their obligations seriously, the state society would have even better executive, public relations, legislative and nominating committees. It is not enough to come to committee meetings. It is not enough even if you stay until the business is finished. You must, in addition, represent the group that sent you here, and moreover, you must represent the state society's point of view when you go back to your district.

One of my objectives has been to develop a more effective democracy in the Society. Every fellow has and *should exercise* his own share of the responsibility. Every district society should be an effective part of the organization. The central committees with district counterparts need the stimulus of initiative from the districts. The district public-relations committees have an obligation to meet the problems of socioeconomic public relations locally, as well as keeping the central committee informed, through the district chairmen, who are their delegates to the state committee, about their local problems and how they are met. Major principles of policy should be cleared through the central committee. Some districts have met and solved problems in a creditable manner but have not adequately reported their experience for the general benefit. Better liaison is needed between cities in the districts, as well as between the district and state societies. Parenthetically, effective interstate liaison offers tremendous values. It seems to me the time is ripe for revival of the New England Medical Council.

I hope that you will not feel it inappropriate for me to record here some personal impressions gained through a relatively active association with medical organization for many years and more especially in the last two years. I have taken my *ex-officio* membership in all committees seriously and have assimilated a point of view that seems worth reporting.

In the past two years a great many doctors have gotten out of the groove of subjective musing into the objective area of thinking and talking in fields relating to the distribution of medical care. There

is a little more evidence of individual initiative and of group initiative from district societies. Recently eighteen state-society presidents met in Michigan at the invitation of the Michigan State Medical Society to consider the desirability of co-ordinating grass-roots planning for realistic approach to problems of unmet needs.

There are some who look with misgiving at any departures from traditional policies. There are some who believe we should ruthlessly discard old ways. These divergencies are the essence of democracy. Leadership should not be too far behind new crystallizing attitudes of less vocal majorities. If the president of the Society can sense definite major trends and feels confident of majority support, he should exercise the initiative that I believe is given him by the Society when he is elected to lead. In these times the attitude of awaiting specific mandates from the formal vote of the Society may be much too slow. I have never hesitated too long to take an action that seemed to me to be in the Society's interest, despite the objections of some men whom I regarded highly. Personally, I believe the American Medical Association is a little too slow in adjusting its policies and activities to crystallizing opinion. The structure of democracy in the organization is there, but too few of the right men are vocal soon enough for efficient evolution. This also applies to society as a whole.

In a recent survey, less than half of twenty-two groups represented in the Massachusetts Central Health Council favored voluntary plans for medical care. How many of these groups have broad enough information to have well-grounded opinions? It is important that we better inform ourselves and contribute to discussions toward legislation that is really in the ultimate public interest.

I shall comment briefly on some of our activities.

Committee on Society Headquarters

We have not yet approached effective development of our central office organization, physically or functionally. It is my hope and expectation that we shall study the organization of other state societies and evolve a more adequate structure to meet the needs of Massachusetts, public and professional. After the present emergency has passed, some of the needs will be easier to meet. But we cannot afford to drift passively along in the meantime.

The functions of the executive secretary have greatly increased this year. He has been utilized by most of the committees, perhaps to the greatest extent by the Committee on Legislation, but this position still is not fully developed. We are growing rapidly and we must be sufficiently alert concerning present and approaching needs of organization.

The office arrangements are not satisfactory and the committee has explored the possibility of getting more space in or outside the library building. More and better arrangements for committee rooms

are needed. We have expended none of our \$1200 budget for headquarters because the committee has not been able to settle on plans.

Committee on Finance

Without the annual meeting this year, we shall not show so favorable a balance as formerly but the Society is in a sound condition financially. No other state society has lower annual dues. I think you ought to know that committee members come from the Cape to the Berkshires — for the most part at their own expense — to do your planning and organizing and to settle your problems. I am sure I spoke for the Society when I vetoed the "Dutch treat" dinners of committees while engaged in Society business.

I hold the conviction that receipts should be ploughed into service for the fellows and the people we serve.

Committee on Legislation

Dr Browne has devoted tremendous energy to the meeting of his obligations. Having myself spent many days at the legislative hearings, my perspective on the relations between doctors individually, doctors organized — the American Medical Association and the Massachusetts Medical Society — and the public has been broadened. We have been misunderstood for years. We have been admonished on numerous occasions by public administrators to come out of our temples and to let the people get to know us better. In matters of legislation, we, as the organization best informed about certain aspects of health, medical education and medical practice, *must* make our position clear to the legislators. They want to know our thought about these things. My respect for legislators has increased through a better understanding of their problems. Some of us have been inclined to forget that the public has a proper interest in fields of medical care. I think I may say that we have opposed some legislation that was supported by highly organized and well financed groups.

The Committee on Legislation has had a very busy year. There are advantages to the present organization of this committee. One member is chosen from each district society and the chairman is elected from this group, but I wonder whether a small executive committee on legislation, selected from the Society as a whole for their special capacity for contact with legislative people, might be of advantage. Contact with the legislator by his family physician could still be done by the district legislative committees.

For the Medical Society of the State of New York, Joseph Lawrence effectively developed and maintained confidence of legislators in that state for twenty-five years. He is now in Washington in a national capacity, conducting a two-way information

One cannot be exposed to public attitudes toward organized medicine at the State House without realizing the need for a better understanding of our motives and objectives.

Subcommittee on Public Information

The Committee on Public Relations has created the Subcommittee on Public Information. This committee has met with important representatives of the press and with radio, advertising and public administrators and has made a beginning this year toward a better understanding of health and distribution of medical care on the part of the public.

We have participated in radio broadcasts with dental, hospital and other groups. We have actively participated in Health Week (May 6 to 12), by radio and press contacts. We have met with the chairman of the Michigan State Society's radio committee to hear of that state's experiments in the field of public information.

There is profit in continuity of discussion of problems in distribution of medical care. Some are impatient because discussions or "conversations" do not yield immediate, definite programs. I have a conviction that unless we have these "conversations," in order to explore untried field of endeavor by group thinking, we shall not make progress toward ultimate solutions.

Subcommittee on Labor and Industry

We have made overtures toward better mutual understanding and expanding areas of agreement with labor through the Subcommittee on Labor and Industry of the Committee on Public Relations. We have also met with certain representatives of industrial management. These meetings have been frank and cordial. I am sure that they have already yielded dividends and will continue to yield profit to the groups involved, moreover, they are exercises in better citizenship.

Committee on Postwar Planning

The Committee on Postwar Planning has made substantial progress toward organizing medical schools and hospitals to meet the needs of returning medical officers. Hospital trustees have already begun to co-operate with the program. This committee is also conscious of the obligation to plan postgraduate extension so as to reach every doctor in the Commonwealth, whether or not they are members of the Society.

The Society can rest assured that its obligations in this field are in good hands. These busy men are applying themselves energetically to the solution of problems that should be actively met. Information about their activities is covered in reports to the Council.

Clinical Information Bureau

The Clinical Information Bureau is expanding its coverage of information in all branches of clinical

facilities for the benefit of every doctor in this state, regardless of whether he is a resident or a member of the Society. The service is used more and more as its value is discovered. It is planned to continue the development of this project under the wing of the Committee on Postwar Planning.

Committee on Publications

The *Journal* continues to justify our pride as one of the best in its field. I am glad to say that its editorial policy is more liberal than that of the *Journal of the American Medical Association*.

I should like to see further excursion into the coverage of news activities of the Society. This year the committees have been extremely busy and have not had reporters to summarize their activities for the proper and adequate enlightenment of the membership. I believe that the *Journal* is the proper medium for this information. We need to develop someone with reportorial instincts to see what goes on and to interpret its significance in a readable manner. Sometimes district-society publications have indicated significantly what might be done. Some policies of these local papers have, however, been contrary to my ideas of what constitutes constructive criticism. *Medical Economics* is still the best source of information and the most universally read periodical we have in this field.

Blue Shield

The Massachusetts Medical Service is the fastest growing plan of its kind in the country. We have more than 130,000 participants, twice as many as when we started the year. Our list of nonparticipating physicians has shrunk considerably. We found a great many of these were in the service or were full-time institution men. There are still some who want to see a perfect plan before they come in. It seems to me that we have the logical answer, and we shall expand as fast as experience seems to justify. There are indications now that, if the present favorable trends continue, we may be able to expand to complete hospital medical-service coverage in six months. I hope to see the local professional Blue Shield committees become more conscious of their opportunities and responsibilities.

Blue Triangle

The Blue Triangle or Bank Plan for financing costs of medical service has been initiated in this state. Because both doctors and bankers are conservative, it is expected this project will not develop like prairie fire. I am convinced that the plan is well conceived and that it fills a need that will be even more apparent after "war prosperity" has passed. The simplicity of the machinery, the low interest rates and the fact that the necessary papers are at the doctor's elbow, ensure ultimate extensive utilization of this plan by a great many

Rationing

Our central and local committees on rationing, with the assistance of the War Participation Committee, have made statesmanlike contributions toward better citizenship of doctors and patients. These excursions into the "policing" field are important and we can look with pride for the most part on our record here. We are showing that when our co-operation is sought and utilized, we earn public respect.

Tax-Supported Medical Care

This field is a large one, and it is a good deal to expect that all the coverage needed will be given by busy doctors. Veterans' medical care will soon be a tremendous problem. This is one of the fields that needs continuity of observation and contact. Perhaps a better informed headquarters staff is the only practical answer in this and some other fields.

Industrial Health

This is another field that is of increasing importance. The American Medical Association has outlined plans for county societies to implement. More energy and time is needed than has been available by specialists. Rhode Island has set us a good example. They are, of course, more highly industrialized in a concentrated area.

Health Councils

Everybody agrees that better organization of district and central health councils is needed. The Massachusetts Central Health Council has a budget of only \$200 a year. Michigan spends \$20,000 a year in this field. This kind of group activity was one of the recommendations of the Committee on the Costs of Medical Care that was endorsed by the American Medical Association. We have toyed with the idea for years, and we do not yet begin to meet our obligations.

Committee on Ethics and Discipline

This committee devotes a great many hours to conscientious and objective consideration of its problems. Because its deliberations are confidential, you hear very little about the work these men do. You can well feel confident that they strike a nice balance between idealism and realism. Defendants are treated with equal consideration regardless of professional prominence.

Committee on Membership

Some criticism has been raised toward this committee because of seeming disregard of recommendations of local membership committees. It may be that in the serious effort to maintain the highest

standards of admission, they have sometimes not given quite enough consideration to local opinion

* * *

In closing I express my deep and sincere appreciation for the loyal support that I have received. It is, more than you know, an enriching experience to be honored with leadership of this society

E S BAGNALL

MISCELLANY

DIABETES AND TUBERCULOSIS

That diabetic patients are prone to acquire tuberculosis is not a new observation, but present-day circumstances have given it a new importance. If the opportunity for effective treatment of tuberculosis is not to be lost, this sinister association must be kept in mind by the doctor. The way to safety lies in considering the possibility that tuberculosis may be now, or at any time may become, a complicating factor with every case of diabetes. The following abstract of a recent paper (Banyai, A L and Cadden, A V. Diabetes and tuberculosis. *Arch Int Med* 74:445-456, 1944) calls attention to the problem

* * *

The significance of the association of diabetes and tuberculosis is accentuated by the continued rise in the frequency of diabetes and the increase in the incidence of pulmonary tuberculosis in persons with diabetes in spite of the decline in the tuberculosis mortality rate in the general population.

Reports from American clinicians made over a period of years indicate that tuberculosis occurs four times as frequently in diabetic persons as in the general population. The age of the diabetic patient is important. One study in Massachusetts showed that tuberculosis was more than thirteen times as frequent among those who acquired diabetes before the age of fifteen as it was among a corresponding group of school children, while among adolescent diabetic patients the incidence was sixteen times as great as that in a corresponding high-school group.

Several theories have been proposed to account for the predisposition of diabetic persons to tuberculosis. Of these the one which the evidence seems to favor is that vitamin A deficiency plays a part. Since a vitamin A deficiency usually occurs in the presence of diabetes, this lack may explain in a large measure the increased susceptibility of diabetic patients to tuberculosis. Lack of vitamin A causes specific pathologic changes in the mucosa of the respiratory system which favor the invasion of bacteria into the lung and bronchial tissues.

A wide discrepancy exists between the estimated number of cases of diabetes associated with tuberculosis and the number of such patients who are admitted to tuberculosis hospitals. Failure to hospitalize these patients in specialized institutions carries serious implications relating to the welfare of the patient and to the public health. The reasons for this failure may be lack of diagnostic consciousness, improper interpretation of symptoms, incomplete diagnostic investigation and asymptomatic forms of pulmonary tuberculosis. The higher recovery rate of persons with early tuberculosis as compared with that of those with advanced tuberculosis justifies a plea for an early diagnosis of this condition in diabetic patients.

Experience has shown that the best attitude is to anticipate the possibility of tuberculosis as a complication. A tuberculin test should be given to all persons with diabetes. This test should be repeated annually as long as it is negative. For those who react positively to tuberculin there should be a chest roentgenogram every year at least. Examination of the sputum should be carried out for all patients with a productive cough and if the roentgenogram of the chest indicates reason for suspicion, fasting stomach contents should be aspirated five successive times and examined by culture or by the inoculation of guinea pigs.

The percentage of diabetic patients entering the tuberculosis hospitals with minimal tuberculosis seems to be

unduly low and may be attributed to a lack of diagnostic suspicion on the part of the physician treating the diabetes. The emphasis formerly placed on the lack of subjective symptoms of diabetic patients with active pulmonary tuberculosis is no longer valid since mass x-ray surveys have revealed that asymptomatic tuberculosis also exists among non-diabetics. Several authors have observed that cavitation is frequent when pulmonary tuberculosis is complicated by the presence of diabetes. Other complications except that of spontaneous pneumothorax occur less frequently than they do in nondiabetic patients with tuberculosis.

The management of diabetes in the presence of tuberculosis has evolved with the trend in diabetic treatment. In the authors' experience it was found that, in patients who were given a well planned diet and adequate amounts of insulin, slight glycosuria and hyperglycemia not exceeding 200 mg per 100 cc are compatible with favorable therapeutic response so far as pulmonary tuberculosis is concerned. Improvement in the pulmonary condition of patients belonging to this group compares favorably with that recorded for tuberculosis patients whose blood sugar was kept on a practically normal level.

Although it may appear heretical in the treatment of tuberculosis the authors are of the opinion that reducing the diet for overweight diabetic patients with pulmonary tuberculosis is as justifiable and practicable as for nontuberculous obese persons with diabetes. The administration of massive doses of vitamin A (150,000 to 200,000 U S P units) daily may serve as a useful adjunct in the management of diabetes mellitus complicated by pulmonary tuberculosis.

The indications and contraindications for collapse therapy are the same for diabetic as for nondiabetic tuberculous patients. Because of the frequency with which empyema complicates artificial pneumothorax in persons with predominantly exudative and caseous tuberculous lesions of recent origin, the use of this measure is rather limited for tuberculous diabetic patients.

An analysis of the reports of ten American clinicians based on the observations of 17,358 cases of diabetes indicates a higher incidence of tuberculosis in diabetic persons than in the general population of the United States.

The fact that an unusually high percentage of diabetic patients who acquire tuberculosis are not adequately treated for their pulmonary disease before it reaches the far advanced stage calls for an urgent revision of the diagnostic approach to this problem.

During the period covered by this study 115 tuberculous diabetic patients were discharged from Muirdale Sanatorium. On discharge 8 of the 17 persons with moderately advanced pulmonary tuberculosis were classified as apparently arrested, quiescent or improved, and 9 were unimproved or had died. Of the 96 persons in the far advanced group, 14 reached the stage where their disease was apparently arrested, quiescent or improved, whereas 82 patients remained unimproved or died. These therapeutic results are less favorable than those recorded for nondiabetic patients with moderately advanced and far advanced pulmonary tuberculosis. — Reprinted from *Tuberculosis Abstracts* (July, 1945)

BOOK REVIEWS

A Textbook of Pathology Pathologic anatomy in its relation to the causes, pathogenesis and clinical manifestations of disease. By Robert A Moore, M D 8°, cloth, 1338 pp., with 513 illustrations. Philadelphia and London W B Saunders Company, 1944 \$10.00

Dr Moore's new textbook of pathology is a distinctly worthwhile addition to medical literature. The book is separated into the familiar divisions of general and special pathology. A number of innovations are noted, as, for example, in the presentation of metabolic disturbances. Illustrations are numerous, well chosen and of high caliber. In addition to gross and microscopic photographs there are radiographs, clinical photographs and reproductions from manuscripts of historic importance. References are adequate in number and in most instances represent excellent selections. Preference has been given to references in the English language and to those which have appeared within the last few years. The book, therefore, may be used with value as a guide to

key papers and monographs. The correlation of physiology, chemistry and clinical medicine with pathology is emphasized throughout. The style is clear. It is perhaps too-objective and factual as though the author had tried hard to withdraw his personality completely from the lines that he has penned.

This is probably the most complete textbook of pathology written for the use of medical students. The author has apparently decided to make his book as inclusive as possible at the expense of detailed consideration of some of the more important pathologic problems. The chapter on Bright's disease and renal insufficiency, for example, contains only seventeen pages, including a historical introduction and the bibliography. Reliance is placed on tabular representation of the important clinical and pathologic features of the various types of Bright's disease as a substitute for detailed discussion.

Treatment of diseases caused by poisonous gases and by various parasites and viral agents is representative of the attempt to present a thoroughly modern textbook. A valuable addition is a brief chapter on the history and scope of pathology, with a well selected list of references for the interested student. Disagreement may be justifiable with the author's choice of emphasis and selection of material for discussion, but this is of interest only to the professional pathologist. Discussion of those diseases beyond the personal experience of the author in most instances represents adequately and fairly the best opinions in the medical literature.

On the whole Dr. Moore has written an excellent, complete and modern textbook of pathology, which should meet the requirements not only of the medical student but also of the physician who seeks brief accurate discussions of pathologic processes. The book is well printed and attractively bound.

Training Medical Secretaries in Junior Colleges. By Evangelin Markwick, Ph.D. 8°, paper, 88 pp., with 12 tables. New London, New Hampshire: Colby Junior College, 1944. No charge.

This study covers a period of nine years in which eleven junior colleges, five hundred and thirty-nine physicians from forty-five states and one hundred and twenty-four medical secretaries participated. The research was limited to training given by junior colleges. The physicians were asked to enumerate required duties in the office and in the laboratory. The medical secretaries who were trained in junior colleges were requested to enumerate various duties performed in their daily work in the office and laboratory. Sixteen comprehensive detailed tables analyze the various duties as shown by the reports of the physicians and secretaries.

An interesting part of this study has to do with working hours, salaries and the personal attributes of medical secretaries. The job specifications made by medical secretaries do not differ essentially from those made by physicians. A large majority of the secretaries, over 77 per cent, reported duties that should classify them as both office and laboratory workers. Four hundred and eighty-two physicians reported that they employed assistants for secretarial and laboratory work. Two hundred and twenty-five of the three hundred and fifty physicians reporting on laboratory training for medical secretaries believe that the duties could be taught in a college laboratory.

This study indicates that a significant proportion of physicians need medical secretaries and believe that colleges with well equipped and properly staffed laboratories could prepare them adequately.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

An Outline of Tropical Medicine. By Otto Saphir, M.D., director, Department of Pathology, Michael Reese Hospital, and professor of pathology, University of Illinois College of Medicine. 12°, cloth, 86 pp. Chicago: The Michael Reese Research Foundation, 1944. \$1.00.

This small manual has been written for physicians who may be brought into contact with tropical diseases under

present conditions. The outline summarizes the barest essentials of the more important tropical diseases. Diseases due to fungi, to vitamin deficiencies and to snake and insect poisonings are not included. Only brief mention is made of diseases caused by animal parasites. Diseases occasionally encountered in the United States, such as amebic and bacillary dysentery, commonly described in any textbook, are omitted. It is hoped that this small volume will serve as a ready reference manual for the general practitioner.

Handbook of Diagnosis and Treatment of Venereal Diseases. By A. E. W. McLachlan, M.B., Ch.B. (Edin.), D.P.H., F.R.S. Ed., clinical medical officer, Joint Committee's Clinic, medical officer-in-charge, Venereal Diseases, Newcastle General Hospital, and lecturer in venereal diseases, King's College, University of Durham. 12°, cloth, 364 pp., with 159 illustrations. Baltimore: Williams and Wilkins Company, 1944. \$5.00.

The British regulations of 1916 define venereal diseases as syphilis, soft sore and gonorrhea. This manual has been evolved from the clinical and systematic instruction of under-graduate and postgraduate students over a period of years. It is written for the general practitioner, and emphasis is placed on the importance of early diagnosis. The book is well printed on good paper with a good readable type.

Escleroses Valvulares Calcificadas. Estudo anatomo-patológico, radiológico e clínico com apresentação de cem casos. By Roberto Menezes de Oliveira, M.D., member, Corpo Médico da Aeronáutica, Brazil. 8°, paper, 154 pp., with 67 illustrations. Rio de Janeiro: Tipografia do Patronato, 1943.

This special monograph on valvular calcification is divided into five parts and a summary. The first part discusses the anatomy and histology of the cardiac valves, the second, the pathological anatomy of calcification, the third, radiography of the diseased heart, the fourth, clinical aspects of the disease, and the fifth, the clinical histories of a hundred cases diagnosed roentgenologically. There is also included the pathological and anatomical study of twenty-five autopsied cases. Appended to the text is a bibliography of twenty-six references, and the work concludes with a summary in English.

Familial Susceptibility to Tuberculosis. Its importance as a public-health problem. By Ruth R. Puffer, Dr. P.H., Tennessee Department of Public Health. 8°, cloth, 106 pp., with 9 figures and 21 tables. Cambridge: Harvard University Press, 1944. \$2.00.

Since 1931 the International Health Division of the Rockefeller Foundation has sponsored the study of tuberculosis in Williamson County, Tennessee. The material collected during this survey has been analyzed by Dr. Puffer in this monograph.

P-Q-R-S-T. A guide to the interpretation of electrocardiograms. By Joseph E. F. Riseman, M.D., associate in medicine, Harvard Medical School, instructor in medicine, Tufts College Medical School, and associate in medical research and associate visiting physician, Beth Israel Hospital, Boston. 24°, cloth, 28 pp., illustrated. Cambridge: Sanborn Company, 1944. \$1.50 (plus postage).

This small booklet is intended for use by the beginner as a practical guide during the actual examination and interpretation of electrocardiographic tracings. It is illustrated with fifty-five tracings.

Outline of the Amino Acids and Proteins. Edited by Melville Sahyun, M.A., Ph.D., vice-president and director of research, Frederick Stearns and Company, Detroit. 8°, cloth, 251 pp., illustrated. New York: Reinhold Publishing Corporation, 1944. \$4.00.

This joint manual written by fourteen chemists outlines in a simple and readable manner the essentials of the chemistry and the biochemistry of amino acids and proteins. An attempt has been made to present a clear and accurate picture of this difficult subject. The authors have refrained from entering into the theoretical controversial aspects of the various theories dealing with the proteins.

(Notices on page xxi)

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SPLENECTOMY FOR ACQUIRED HEMOLYTIC JAUNDICE IN THE AGED*

Report of a Case

DAVID F JAMES, M D,† AND LLOYD R EVANS, M D †

BOSTON

A PATIENT who develops severe hemolytic anemia at the age of seventy and has no past history of this disease presents complex problems in diagnosis and treatment. The age of onset is late for the diagnosis of congenital hemolytic jaundice and, regardless of the diagnosis, the question arises whether splenectomy is advisable at this age. Furthermore, increased fragility of the erythrocytes may be overlooked when the routine test for fragility is done on blood samples showing marked anemia. These problems were met in a seventy-year-old woman in whom splenectomy was performed with recovery. The literature was reviewed to determine the usefulness of splenectomy in the treatment of acquired hemolytic jaundice in patients with the onset of the disease occurring after the age of fifty.

CASE REPORT

M E F, a 70-year-old, married woman, was admitted to the Peter Bent Brigham Hospital for the first time on April 15, 1941. The chief complaint was weakness of 3 to 4 months' duration. The family history revealed no case of anemia, jaundice or endocrine disorders, the mother and only brother had suffered from heart disease. The patient had lived in New England all her life, had never been pregnant and gave no history of exposure to any materials known to be injurious to the blood or blood-forming tissue. Systemic review disclosed that the patient's health had always been good in the past.

Four months prior to admission the patient first experienced malaise, increased weakness, fatigability, palpitation and shortness of breath on exertion. She did not complain of paresthesias and gave no evidence to suggest blood loss, bleeding dyscrasia or liver disease. A month later she consulted a physician on account of these complaints. Not until 2 weeks before admission did the skin assume a yellow tint and her physician discover a low red-cell count. Bed rest and the administration of liver extract by mouth during 2 weeks brought no improvement.

On admission the patient appeared to be severely ill, as evidenced by prostration, tachycardia, pallor and a lemon-yellow skin. The tongue was smooth and pale. There was a palpable lymph node in the left supraclavicular region. The blood pressure was 130/40. The heart was slightly enlarged to the left, and there was present a loud blowing systolic murmur, heard best over the cardiac apex. The liver extended 2 cm below the right costal margin, and the spleen was barely palpable. Neurologic examination revealed no abnormalities.

Significant laboratory data included negative Wassermann and Hinton blood tests. The urine was normal except for a + test for protein. The red-cell count was 870,000, with 17 per cent reticulocytes. The white-cell count was 17,500, with 75 per cent neutrophils, 19 per cent lymphocytes, 4 per cent monocytes and 2 per cent unidentified cells, 2 normoblasts were found among 100 leukocytes. The hemoglobin was 32 per cent (Sahli). The icteric index was 20, and by the Sanford¹ method of erythrocyte fragility determination, hemolysis began at 0.44 per cent saline solution and was complete at 0.42 per cent, a normal result by the method used.

When correction was made for the anemia,² the initial hemolysis was found to occur at 0.58 per cent saline solution, whereas a normal control showed the same amount of hemolysis in a 0.44 per cent solution. There was 75 per cent hemolysis in 0.40 per cent saline in the blood, the same degree of hemolysis occurred at 0.35 per cent saline in the blood of the normal control. In addition, the patient's blood gave a negative hemolysis test with acidified serum³ and contained no hemolysins of the Donath-Landsteiner type, no auto-hemolysins and no agglutinins in the presence of cold or heat. Plasma hemoglobin amounted to less than 7 mg per 100 cc, and was considered normal. At that time (3 weeks after admission) the red-cell count was 1,200,000, with 4.9 gm of hemoglobin per 100 cc, and 29 per cent reticulocytes. The hematocrit reading was 16.6, the mean corpuscular volume 138.3 cubic microns, the mean corpuscular hemoglobin concentration 30 per cent, and the mean corpuscular hemoglobin 42 micromicrogm. The white-cell count was 13,600 with 54 per cent segmented neutrophils, 13 per cent band forms, 4 per cent eosinophils, 21 per cent small lymphocytes, 4 per cent large lymphocytes, 3 per cent adult monocytes and 1 per cent young monocytes. A smear showed moderate anisocytosis, macrocytes and normocytes were seen. There was much polychromatophilia, with some Howell-Jolly bodies, stippling and a few erythroblasts and normoblasts. No spherocytes were seen. The platelets and white cells were normal. A direct van den Bergh test showed 0.9 mg of bilirubin per 100 cc of plasma and an indirect one 3.1 mg §. Roentgen-ray films of the chest, gastrointestinal tract, skull and long bones failed to disclose disease. Gastric aspiration revealed free hydrochloric acid to the extent of 22 units in the sample withdrawn 20 minutes after histamine injection.

Following the injection of six doses, totaling 8 cc, of liver extract (Lederle, N N R) and a transfusion of 500 cc. of whole blood, the red-cell count was only 1,430,000, with no increase in reticulocytes. The hematocrit reading was 19, and the icteric index 30. The patient felt improved and was discharged home on May 13, approximately 1 month after admission.

After spending a week at home the patient became so chronically exhausted that she was readmitted. Physical examination at that time was essentially the same as before. The red-cell count was 1,020,000, the hemoglobin 3.75 gm per 100 cc, the hematocrit 12, and the icteric index 18. The white-cell count was 33,100, with a normal differential ex-

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§The determinations listed were made by Dr. Henry H. Brewster and Miss Geneva A. Daland of the Thorndike Memorial Laboratory, Boston City Hospital.

cept for 4 per cent normoblasts and 1 per cent megaloblasts. The fragility of the erythrocytes was again studied. By the method of Sanford, hemolysis began at 0.44 per cent saline solution and was complete at 0.34 per cent, both values being within the limits of normal and equivalent to those of a normal control blood tested at the same time. When, however, enough plasma had been removed from the blood of the patient to make the hematocrit reading normal—that is, 40—and the fragility was again tested by the Sanford method, it began at 0.50 per cent and was complete at 0.40 per cent, values definitely indicative of greater fragility than normal. In order to check the findings of these naked-eye tests, the photoelectric method of Hunter⁴ was used, testing blood with a hematocrit level of 17. When fragility was determined by this method, hemolysis began at 0.60 per cent saline and was complete at 0.36 per cent, whereas in the normal control it began at 0.48 per cent and was complete at 0.34 per cent.

During this stay roentgen-ray therapy—two doses of 25r each directed at the entire trunk on successive days—was administered on the supposition that the etiologic process might be neoplastic in nature, and was followed by a fall in the white-cell count from 25,000 to 11,000 and a decrease in reticulocytes from 18 to 6 per cent. It was therefore discontinued. Twelve days and 29 days later the reticulocytes numbered 6 per cent and 9 per cent, respectively.

On June 8, 3 weeks after admission, the patient experienced an attack of severe pain in the right upper quadrant of the abdomen. A mass in the right upper quadrant, corresponding to the gall bladder, became palpable and remained so for 24 hours, after which it could no longer be felt. The findings were interpreted as indicative of obstruction of the cystic duct. Biopsy of the palpable left supraclavicular lymph node revealed tuberculous lymphadenitis. On the 24th day, a biopsy of the sternal bone marrow was performed and was interpreted as showing hyperplasia of the marrow, chiefly erythroblastic in nature, and probably secondary in origin.

Because of the above findings and the failure of the patient to improve on vigorous transfusion therapy,—she received a total of 7600 cc of whole blood in 1 month,—she was transferred to the Surgical Service for splenectomy. On June 29, the day of her transfer, the red-cell count was elevated to 2,100,000 by repeated transfusions. The following day splenectomy was performed, the patient withstanding the procedure well. She received two more transfusions on the day of operation. On the first postoperative day the red-cell count was 2,600,000. No further transfusions were given.

At operation the gall bladder was seen to be tense and distended. It did not empty on pressure, no stones could be palpated. It was not removed. The liver did not appear abnormal to inspection or palpation. The weight of the spleen was 362 gm. Following is the report on the pathological examination of the spleen.

The color of the cut surface is dark red. The malpighian bodies are not prominent. There is no grossly evident increased trabeculation. No areas of infarction are encountered. Microscopical examination discloses that the capsule is not remarkable. The malpighian corpuscles are essentially normal in color and size. They are quite active, with sometimes moderately prominent germinative centers. The reticular cords, however, show definite lymphoid depletion, and there is a certain degree of engorgement of the meshes of the red pulp. One of the most striking features is the presence of large amounts of golden-brown pigment consistent with hemosiderin. This is found extracellularly as well as intracellularly. In the latter instance it is within large monocytes, or often within the lining cells of the sinuses. Scattered through the organ there appear to be a somewhat increased number of polymorphonuclear leukocytes. Another striking feature is the presence of foci of hematopoiesis mostly situated near the malpighian corpuscles, and there is also hematopoiesis going on within the sinuses. The number of eosinophilic myelocytes is quite excessive, and occasional megakaryocytes are encountered. The general architecture is well preserved. The sinuses are frequently prominent. The large arteries show only a minimal degree of sclerotic changes, whereas the small arterioles are rather uninvolved. This picture of marked hematopoiesis

with extensive hemosiderin deposits is quite consistent with that of a hemolytic anemia.

After an uneventful postoperative course of 11 days, the patient was transferred to the Medical Service, at which time the red-cell count was 3,500,000. She appeared much stronger and happier than at any previous time during the hospital stay. When she was discharged on the 22nd postoperative day, she was ambulatory and the red-cell count was 4,300,000, with 11.5 gm of hemoglobin per 100 cc, 26 per cent reticulocytes and an icteric index of 14.

The patient was seen again 4 months after splenectomy, at which time she looked well and had regained her strength so that she was able to arise at 5.30 every morning. No pallor or jaundice could be detected. The red-cell count was 4,560,000, with 13.5 gm of hemoglobin per 100 cc. The white-cell count was 8400, with 36 per cent segmented neutrophils, 1 per cent band forms, 52 per cent lymphocytes, 8 per cent monocytes and 3 per cent eosinophils. There were 0.5 per cent reticulocytes. Platelets were plentiful, and the blood smear appeared normal except for the variations in red-cell size described below. No spherocytes were seen.

Fragility tests done by the photoelectric method of Hunter disclosed that the red cells were still definitely more fragile than those of a normal control. In 0.60 per cent saline solution 5.4 per cent of the erythrocytes were hemolyzed, whereas hemolysis did not begin in the control blood until the hypotonicity of the salt solution had reached 0.51 per cent. Ninety-eight per cent of the cells were hemolyzed at 0.36 per cent saline, whereas but 87.5 per cent hemolysis occurred in the blood of the control at this concentration. Fragility tests performed on the blood of the patient's sister and grandnephew, the only relatives available, failed to reveal aberrations from the normal.

A Price-Jones curve showed a range of red-cell diameters considerably wider than normal. Of 500 erythrocytes examined, one had a diameter of 3.1 microns, one of 3.5, one of 3.9, and 22 of 4.2. The peak of the curve occurred at 7.0 microns. There were 11 cells with a diameter of 9.1 microns, and 4 with a diameter of 9.8. Price-Jones curves done on the blood of the patient's sister and grandnephew failed to reveal abnormalities.

On March 16, 1942, over 8 months after splenectomy, the patient reported that she was entirely well and more vigorous than she had been at any time in the previous 10 years.

DISCUSSION

This case yields information on three phases of the diagnosis and treatment of hemolytic jaundice. First, the disparity among results obtained with various types of erythrocyte fragility tests deserves comment. Second, an attempt to classify the patient's anemia as either the congenital or the acquired form helps to evaluate recent studies of certain features of these syndromes. Third, the patient's advanced age at the time of onset and of splenectomy is of interest, since only 1 other case of splenectomy for hemolytic jaundice in a patient over seventy years of age has been found in the literature.⁵

Estimation of Erythrocyte Fragility

The Sanford red-cell fragility test, although widely used and usually adequate for the detection of gross changes, gave an erroneous result in this case in the presence of marked anemia. Although a large percentage of the red cells were abnormally fragile, the anemia was so marked that the quantity of blood used in the test did not contain enough such

is to produce hemolysis detectable to the eye. When, however, the anemia was corrected by removing sufficient plasma to bring the packed red-cell volume to a normal level, the abnormal fragility of the cells was immediately apparent.

In anemic cases it is not necessary to bring the red-cell volume to normal before determining the fragility of the erythrocytes if the method used in estimating the percentage of the cells hemolyzed by the various concentrations of saline solution is sufficiently accurate. The fragility test as adapted by Hunter⁴ to the photoelectric colorimeter meets this requirement. A minor modification of this method was made to save time. Constant and reliable values could be obtained by mixing the various dilutions of saline solution with blood in Klett-Summerson colorimeter tubes, centrifuging at 3000 r p m for twenty minutes and measuring directly the amounts of hemoglobin in these tubes without decanting the supernatant into other tubes. No ammonium hydroxide was added.

Diagnosis of Congenital and Acquired Hemolytic Jaundice

The natural history of classic congenital hemolytic jaundice is well known. Typically there are episodes of anemia, acholuric jaundice, notable splenic enlargement and upper-abdominal pain from cholelithiasis. Whereas the symptoms tend to appear and disappear, the following signs persist throughout microspherocytosis with increased fragility of the erythrocytes in hypotonic saline solutions, accompanied by anemia, reticulocytosis and increased urobilinogen content of feces. The disease frequently manifests itself in childhood or early adulthood, but may never be detected. Although the past history and family history may not reveal the presence of any of these features, blood studies of relatives of patients with this disease frequently demonstrate increased fragility, which is inherited as a mendelian dominant.⁶ Many cases remain entirely asymptomatic throughout life, a few develop in older age groups. This work indicates that a case of hemolytic jaundice should not be termed congenital until evidence is found in the family of characteristic symptomatology or of microspherocytosis or increased red-cell fragility. The discovery of any or all of these characteristics in the blood is not enough to make the diagnosis certain. Meulengracht, cited by Dameshek and Schwartz,⁷ denied that increased saline fragility was pathognomonic of congenital icterus, and reported cases of the acquired type with increased fragility. Furthermore, he stated that an inherited disturbance in formation was only one of the causes of increased fragility of the erythrocytes, and that actually the increase might be regarded as a regeneration phenomenon or as a sign of the action of toxic or hemolytic forces on the red cells in the circulation. Ham and Castle⁸ comment on the

effect of erythrostatics in the spleen and other organs to increase erythrocyte fragility in presumably otherwise normal persons. They report on the transient but striking increase in fragility that occurred in 5 cases of severe acute hemolytic anemia observed following the administration of sulfanilamide. This was so great that some of the red cells in venous samples were hemolyzed in isotonic or only slightly hypotonic saline solution. These authors believe that erythrostatics occurring in the spleen and other organs was "presumably operative" in bringing about the increased fragility. Watson⁹ refers to 2 cases classified as macrocytic hemolytic anemia in association with liver disease that exhibited decreased resistance of the erythrocytes to hypotonic saline solution, without spherocytosis. These data demonstrate the difficulty in determining the fundamental nature of a hemolytic jaundice from fragility studies alone.

Singer and Dameshek¹⁰ report a series of cases of so-called "symptomatic" hemolytic anemia, occurring in conjunction with other diseases (dermoid cyst in the ovary, chronic lymphatic leukemia, Hodgkin's disease, lymphosarcoma, severe liver disease and pneumonia with a panagglutinin). In these cases spherocytosis and increased hypotonic saline-solution fragility were frequently present. In the case associated with dermoid cyst in the ovary, splenectomy had a transient effect on the hemolytic jaundice, but removal of the tumor itself was marked by general improvement, subsidence of spherocytosis and a return of erythrocyte fragility to normal. Haden¹¹ also states that spherocytosis may occur in hemolytic anemia other than congenital hemolytic jaundice, reporting that it may be the result of leukemia, Hodgkin's disease or acetylphenylhydrazine poisoning. All these data indicate that a diagnosis of congenital hemolytic jaundice may not be made solely on the basis of laboratory findings in the blood of the patient.

In the case described we were not able to make a diagnosis, either preoperatively or postoperatively, of hemolytic jaundice of proved congenital origin. The most cogent points that argued against the congenital type were three in number. First, the history was not typical of the congenital form, with the sudden appearance of severe hemolytic anemia in old age. Second, there was no history among the patient's relatives of any condition resembling hemolytic jaundice, and the available relatives gave no laboratory evidence of the hematologic characteristics of this disease. Finally, the microscopic examination of the spleen was not characteristic of congenital hemolytic jaundice.¹² The pulp was only moderately filled with erythrocytes, the malpighian corpuscles were not obscured, and there was present an abnormal degree of phagocytosis. Therefore, the diagnosis made was relatively acute hemolytic anemia of the acquired variety. Since this diagnosis was made by exclusion, we cannot be certain that

our case was of the acquired variety any more than a disease can be called "acquired" unless a definite etiology can be established. It is concluded, however, on the basis of the data outlined above that the probability of its being acquired is great.

Acquired hemolytic anemia represents a heterogeneous group of cases, and may be broken down, for purposes of classification and therapy, into two subdivisions: those of known etiology and those whose etiology is unknown. Among the known causes are poisoning with such drugs as sulfan-

have no remedial effect on this patient's acquired hemolytic jaundice, made it seem advisable to try all other reasonable therapeutic measures first. Intensive liver and iron therapy, intensive transfusion therapy (which was marked by an increasing frequency of reactions) and roentgen-ray therapy directed at the trunk, however, were ineffective or of no permanent benefit. Splenectomy, on the other hand, proved effective.

Subsequent study of the literature revealed 15 patients, including the one here reported, in whom

TABLE 1 *Splenectomy Resulting in Definite Improvement*

CASE No	SOURCE	AGE AT ONSET	RED-CELL FRAGILITY	SPHEROCYTOSIS	RESULTS OF SPLENECTOMY	PATHOLOGICAL REPORT ON SPLEEN
1	Mandelbaum ⁵	75	Normal at onset, later increased preoperatively and postoperatively	Present	Slow but steady improvement	Weight, 650 gm., thickened trabeculae, reticuloendothelial elements increased, sinuses distended and lining cells prominent; much extracellular and intracellular iron-containing pigment.
2	Israels and Wilkinson ¹³ (Case 2)	57	Increased	Present	Slow but steady improvement	Weight, 700 gm., no increase in connective tissue; sinuses dilated, histiocytes remarkably prominent in pulp; erythrocytes very scanty.
3	Davidson and Fullerton ¹⁴ (Case 6)	60	Normal	Absent	Good recovery during bronchitis 4 years later; the patient was mildly jaundiced.	Malpighian corpuscles smaller than usual and widely separated owing to an increase in pulp, which was due to an excessive number of red cells; findings consistent with usual findings in acholuric jaundice.
4	East ¹⁵	52	Normal preoperatively; slightly increased postoperatively	Not mentioned	Slow but steady improvement	Weight, 600 gm., normal malpighian corpuscles, hyperplastic endothelium, whose cells contained large iron-bearing granules, phagocytosis of red cells and occasional giant cells.
5	James and Evans	70	Normal by ordinary methods; increased if corrected for anemia, preoperatively and postoperatively	Absent	Good recovery	Weight 362 gm.; marked hematopoiesis with extensive hemosiderin deposits both within and without cells; normal malpighian corpuscles.

ilamide,⁸ acetylphenylhydrazine¹¹ and others. Also, this syndrome may occur in conjunction with other diseases, notably lymphomatous neoplasia.^{10, 11} Still other cases occur without any pathologic accompaniment. As has been stressed above, increased erythrocyte fragility and microspherocytosis may be found in any of these types of acquired hemolytic jaundice, although less constantly than in the congenital form.

Splenectomy for Acquired Hemolytic Jaundice in the Aged

Splenectomy is attended by greatly increased risk when performed, for whatever reason, on aged persons.⁷ This fact, together with the distinct possibility that the removal of the spleen might well

the onset of hemolytic jaundice occurred at or beyond the age of fifty, and in whom not all the essential criteria for a diagnosis of congenital hemolytic jaundice, as discussed above, were present. About half these were patients in their fifties. Two had passed their seventieth birthday at the time of onset, the patient here described being seventy and another being seventy-five. The family and past histories were noncontributory. Symptoms and physical signs — which were of no differential diagnostic or prognostic import — included loss of energy, anorexia, weakness, palpitation, shortness of breath on exertion, pallor, jaundice and enlargement of the liver and, somewhat more regularly, of the spleen.

Of the 15 cases, 5 showed definite improvement

ter splenectomy These 5 cases comprised the 2
er seventy years of age, 1 in the sixties and 2 in
the fifties The essential data are summarized in
Table 1 It is interesting to note that in only 1 of
these cases (Case 3) was there a pathologic picture
like that seen in congenital hemolytic jaundice In
this case fragility of the red cells was said to be nor-
mal, and spherocytosis was not mentioned In the
other spleens a marked increase in the number and
activity of reticuloendothelial elements was found
In 10 of the cases reported in the literature
splenectomy was ineffective or resulted in accelera-
tion of the downhill course Of these, 6 are sum-
marized in sufficient detail to make an analysis
valuable (Table 2) It will be noted that in but 1

erythrocyte fragility have a better prognosis than
do those with normal fragility In the group of 5
cases showing improvement after splenectomy, 2
showed increased fragility preoperatively In 2
others the fragility, although reported as normal
before operation, increased after recovery It
is probable that in the studies made before operation
the presence of anemia masked the increased fragility
of the erythrocytes In the group of 6 cases
analyzed in which splenectomy failed to result in
improvement, 3 showed increased erythrocyte
fragility It is impossible to say how many more
of these might have manifested increased fragility
had more accurate methods been used

The cases reviewed from the literature, as well as

TABLE 2 *Splenectomy Without Improvement*

CASE No	SOURCE	AGE AT ONSET	RED-CELL FRAGILITY*	RESULTS OF SPLENECTOMY	PATHOLOGICAL REPORT ON SPLEEN
1	Watson ⁹ (Case 74)	67	Increased	Atelectasis and death on 3rd postopera- tive day	Weight, 880 gm sinuses markedly dilated †
2	Davidson and Fullerton ¹⁴ (Case 9)	51	Normal	Blood count pro- gressively decreased with death 10 days postoperatively	Weight 815 gm. marked prolifera- tion and activity of reticuloendo- thelial system definite myeloid metaplasia findings said to be "typical of reticuloendotheliosis"
3	Thompson ¹⁶ (Case 33)	63	Normal	Death 6 wk. postopera- tively autopsy no aid in diagnosis	Weight, 680 gm evidence of marked blood formation
4	Davidson ¹⁷ (Case 5)	55	Normal	Reticulocytosis persist- ed death 10 mo later of anemia	Weight 1700 gm histiocyte pro- liferation and myeloid metaplasia characteristics of congenital hemo- lytic jaundice absent.
5	Davidson ¹⁷ (Case 9)	58	Increased	Congestive heart failure 36 hr. postopera- tively red-cell count 470 000 at time of death	Weight 820 gm pulp contained in- numerable red cells without marked dilatation of sinuses the appearances were said to be "those of acholuric jaundice."
6	Rastetter and Murphy ¹⁸ (Case 2)	53	Slightly increased	Icterus anemia and re- ticulocytosis re- turned after 1 mo improvement death 2 wk. later	Weight 560 gm section showed dark red pulp with faintly visible follicles marked congestion of sinuses reticulum cells scant.

*No spherocytes were found in any of the cases listed in this table.

†This patient also had hepatic cirrhosis

of these cases (Case 5) did the spleen show a micro-
scopic picture like that of congenital hemolytic
jaundice. This patient died of obvious congestive
heart failure thirty-six hours postoperatively It is
probable that there was not time for the effect of
splenectomy to be demonstrated The remaining
4 cases, which are not included in Table 2, were
reported by Dameshek and Schwartz⁷ and are those
of acute acquired hemolytic anemia in all of which
operative death occurred The ages in these cases
ranged from fifty to sixty-four

In 6 of these 10 cases, the primary cause of death
was found to be closely related to the operative
procedure, whereas in 3 the blood dyscrasia itself
was the principal lethal agent One patient died six
weeks after operation, and autopsy did not help to
make a diagnosis Presumably this death also was
related to the hemolytic process

The question arises whether cases with increased

the one reported here, demonstrate that splene-
ctomy may save the lives of elderly patients with
acquired hemolytic jaundice, and that it should not
be regarded as a useless procedure Although good
results following splenectomy are likelier in a patient
with increased erythrocyte fragility, spherocytosis
and a spleen typical of congenital hemolytic jaun-
dice than they are in others, it is sometimes of value
in patients whose clinical picture lacks one or more
of these characteristics

SUMMARY

A case of severe acquired hemolytic jaundice with
onset at the age of seventy, apparently cured by
splenectomy, is presented

The technic of determination of erythrocyte
fragility is discussed The shortcomings of widely
used methods are pointed out, and the advantages

of recent improvements devised by various workers are described

The differential diagnosis of hemolytic jaundice is discussed, with special reference to the diagnostic import of abnormally fragile red cells and of microspherocytosis

From the literature are reported 14 other cases of acquired hemolytic jaundice, with onset after the age of fifty in which splenectomy was performed. Factors influencing the course of these cases are presented

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THE DEVELOPMENT OF THE STATE CHILD-GUIDANCE CLINICS IN MASSACHUSETTS*

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THE Commonwealth of Massachusetts was the first state to provide by legislation (in 1922) for a division of mental hygiene,¹ with the establishment of child-guidance clinics financed by state funds as one of its major activities. A review of the diversely related developments in psychiatric therapy that culminated in the child-guidance movement shows the state guidance clinics emerging at the peak of the mental-hygiene movement as the logical but unforeseen outcome of efforts to promote mental health by preventive and early correctional treatment.

The mental-hygiene movement expanded with remarkable rapidity through the years 1912 to 1922 under the impact of new psychiatric concepts of mental disease and an increasing revelation of the importance of flaws of personality in precipitating breakdowns in adult life.

A concurrent stimulus was contributed through the adoption by mental hospitals of social services, which brought to light many pertinent aspects of life experiences of patients by means of investigations in the homes and collaboration with local agencies. This type of social service rapidly developed into a specialized profession forming a connecting link be-

tween the hospitals and the communities that they served, and providing a valuable medium for the interpretation of the principles of mental hygiene to the lay public. By 1922, Massachusetts was considered a leader in the new field of psychiatric social service, and trained workers were in great demand by other states.² This expansion of community services was facilitated by the establishment of outpatient clinics for supervision of released patients. These clinics soon became centers for treatment of noncommittable patients, among whom were some children, chiefly delinquents.

In 1919, the General Court of Massachusetts made obligatory the examination of all school children who were three-years retarded, and the formation of special classes where ten or more such children were found.³ The examining service was provided by the state hospitals and the Walter E. Fernald State School (for the feeble-minded) by means of clinics distributed through the Commonwealth and called "traveling school clinics." The impetus that this procedure gave in the direction of child guidance was incalculable and proved to be a most notable contribution to the program of mental hygiene. Although the service was at first viewed by school boards with suspicion and fear of increased expense for special classes, it quickly demonstrated its value, and schools began to refer

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many children whose difficulties proved to be due not to mental deficiency but to physical or environmental handicaps

By 1920, in addition to the traveling school clinics, a number of outpatient mental-hygiene clinics were well established, giving service to adults and children. Northampton had four clinics, and Gardner three. In 1921, Monson had four, Danvers seven, and Taunton two, and Worcester had opened such a clinic at the Summer Street Department.⁴ At that time, the Boston Psychopathic Hospital was established as an independent unit for screening of committable cases and furnishing treatment for milder forms of mental illness. The latter service was in immediate demand and was faced with problems from infancy to adulthood.⁵

By acts of 1921 and 1924, the Division for the Examination of Prisoners was established and financed by the Commonwealth, and was completely equipped with psychiatric and social services.

The case histories in all these different fields presented striking similarities of etiologic factors and unmistakable indications that the most fertile field for mental hygiene lay in the realm of childhood. Meanwhile sporadic experiments in specialized clinics for children were being made throughout the country, chiefly directed toward the treatment of delinquency. In 1922, a series of demonstration clinics was planned by the National Committee for Mental Hygiene through its Division for the Prevention of Delinquency. This was financed by the Commonwealth Fund on a five-year plan, and the clinics were located in eight specially selected cities. Of these eight clinics, four survived the exigencies of pioneering, another was subsequently resuscitated, and another was reorganized by two communities, resulting in seven established clinics. The chief problem was the continued financing after termination of the demonstration period. Results of therapy with adjudged delinquents were discouraging, but again the signposts pointed toward earlier recognition and treatment of maladjusted children.⁶

In this preliminary period, prior to 1922, one phase of clinical procedure was worked out that has remained standard to date, namely, the professional clinic team of psychiatrist, psychologist and psychiatric social worker. Although many variations of responsibility have been used, in actual practice each has been found to have its indispensable contribution toward the evaluation and treatment of cases, and the combination has proved more effective than the efforts of any one type of worker.

In Boston, in November, 1921, Dr. Douglas A. Thom was asked to make a survey of one of the health clinics of the Baby Hygiene Association of Boston to determine whether a psychiatrist might have something to contribute to the clinics' program of preventive medicine.⁷ From misgivings concerning the possibility of accomplishing anything with

these immature patients, Dr. Thom was quickly converted to enthusiasm for the rich field of opportunity that opened before him.⁸ Soon three clinics for young children were put in operation under his direction by the Community Health Association (visiting nurses), and were called "habit clinics" as an innocuous but descriptive name. These seemed to be the first clinics in the country that were established specifically for psychiatric therapy for young children.⁹ With startling clearness, the social evils of poverty, disease, ignorance and vice came into focus as the ravagers of childhood and the breeding ground of mental disease.

In 1922, Dr. George M. Kline, with Dr. Thom and other leading psychiatrists, spurred on by the ominous crowding of the state hospitals, presented to the Legislature a preventive program and secured the establishment of the Division of Mental Hygiene, under the Department of Mental Health, with Dr. Thom as director. The division was charged with the responsibility for "all matters affecting the mental health of citizens of the Commonwealth, investigation of causes and conditions that tend to jeopardize mental health."¹⁰ State funds were appropriated for research and for children's clinics.

In 1923, three clinics* were opened in Boston, by the Division of Mental Hygiene and were promptly utilized by children's agencies, visiting nurses and family-welfare workers. In this year also, the Worcester State Hospital established a habit clinic for children such as had previously been seen at its Psychiatric Clinic.¹¹ This clinic was later discontinued and the children were seen at the Memorial Hospital.¹² In 1924, four additional clinics were started by the division.[†] The clinic in the West End (Boston) is still flourishing, having given twenty years of service to a wide area. Two years later the Lynn Clinic was transferred to the auspices of the Danvers State Hospital in order that the clinic staff of the division might be available for a new clinic at Quincy. The Springfield Clinic, which was started as a demonstration clinic because of its distance from Boston, was assisted by private agencies after one year of operation and received general supervision from the Monson State Hospital.[‡]

The initial work of projecting clinics in new communities was undertaken jointly by the division and the Massachusetts Society for Mental Hygiene,¹⁴ which has carried on an aggressive and effective program since the beginning of the movement.

*The first of these was established on June 6 at the Maverick Dispensary, East Boston. It was transferred to the auspices of the Boston Psychopathic Hospital on July 2, 1924. The second was begun on June 8, 1923 at the North End (Boston) Health Unit. It was closed in July, 1928 and reopened in October, 1928, at the North Bennet Street Industrial School. It was consolidated with the West End Clinic in October, 1929. The third was established on October 25, 1923 at the Roxbury Neighborhood House and was closed on September 18, 1924.

†The first was opened on January 12, 1924 at the West End Health Unit, West End (Boston) the second on March 5, 1924 at the Lynn General Hospital (transferred to the Danvers State Hospital on March 30, 1926) the third on April 25, 1924, at the Lawrence General Hospital (transferred to the Danvers State Hospital on March 5, 1940) and the fourth on October 24, 1924 at Springfield (transferred to the supervision of the Monson State Hospital on October 31, 1925 and reorganized with community support on November 20, 1938).

Opportunities were sought for talks and conferences, and when sufficient interest was aroused a sponsoring group was organized to promote publicity, find accommodations and consult with the clinic team on community problems. Theoretically, all the clinics set up by the division were for demonstration, and were eventually to be turned over to hospitals or private organizations. This plan has been carried out except in communities easily available from Boston.

In 1925, four more clinics were in operation.* The clinic at the Boston Dispensary became a part of the Children's Department of this hospital, and in 1933 service was extended to two sessions weekly and the clinic provided training in child therapy for medical interns. The Lowell Clinic also started in a local general hospital, but after two years gave over its patients to a private clinic in the community. Four years later, at the request of schools and agencies, it was reopened and has continued service to date. The Reading Clinic was opened as a monthly diagnostic service for the school department, and in 1931 service was extended to weekly sessions for child guidance and treatment. After a period of full activity conditions changed, and it was closed in 1939 because of decreasing community interest and pressing demands for service by the City of Brockton. The Beverly Clinic also gave diagnostic service until 1931, when it became well established as a weekly guidance clinic. It was taken over by the Danvers State Hospital in 1932.

The Out-Patient Department of the Worcester State Hospital was reorganized during 1925¹⁵ to provide more specialized treatment for children attending the Psychiatric Clinic at the Memorial Hospital.

Already various patterns were emerging among these pioneer clinics. Demonstration clinics had been taken over by the staffs of the state hospitals, communities had rallied to financial support to obtain increased service, clinics housed in hospitals had begun to function as training centers, schools had begun to use clinics for the solution of problems, and contacts with children had contributed valuable information to psychiatrists. The child-guidance movement had won prestige both in professional and in popular esteem.

In 1926, the division started the Quincy Clinic,† which proved to be one of the most successful and is still in the process of expansion. It serves a wide circle of surrounding towns and receives a large percentage of its cases from public schools. For a

few years, it attempted to meet the pressure by using a double staff, then increased service to two sessions weekly in January, 1943, and is now in the process of obtaining community funds for enlarged scope through the interest of a local sponsoring committee.

In Worcester a clinic for children was organized¹⁶ during this year under the name of the Child Guidance Clinic and embarked on its eminently successful career. In the following two years, community interest and support increased so that in 1929 it was able to offer full-time service with the financial participation of the Child Guidance Association of Worcester.¹⁷

At that time, the traveling school clinics began to be under continual pressure to furnish treatment as well as diagnostic service to children who were not defective but who were in need of help, and many cases of this type were served.¹⁸

The year 1927 saw eight clinics of the division and five clinics of the state hospitals well under way. Methods used in Massachusetts were being studied and adopted by other states and other countries.¹⁹ Inquiring visitors were frequent. Schools of social work had co-operated since 1923 in offering related courses and were sending students to the clinics for field training. Social workers were eager to enter the field, but the demand for trained personnel far exceeded the supply.

During 1927, the Taunton State Hospital opened a clinic at the hospital and also one for adults and children at the Sturdy Memorial Hospital in Attleboro.

On December 1, 1927, the Habit Clinic at the New England Hospital for Women and Children in Roxbury, which had previously been conducted under private auspices by Dr. Thom, came under the jurisdiction of the division. This clinic worked in co-operation with the hospital and served a large residential district in the southern section of Boston. It was chiefly a treatment clinic, holding one session weekly and maintaining quite steadily an average attendance of 10 cases per session over a period of sixteen years, until it was consolidated with the Southard Clinic in October, 1943.

In July, 1928, a new venture was initiated²⁰ giving clinic service monthly to tuberculous children at the North Reading Sanatorium. A careful survey was made for the purpose of improving educational facilities, resulting in the introduction of occupational therapy. Considerable social case work was done in co-operation with the Department of Public Health. Owing to the pressure of work in community clinics, this service was changed in 1939 to a consultation service on call.

In October, 1929, the division organized another community clinic in Norwood, sponsored but not financed by an active group of social-minded women. It was housed at the Norwood Hospital and served towns and rural districts to the south and west of

*One of these was opened at the Boston Dispensary on December 5, 1924, and was consolidated with the Southard Clinic at the Boston Psychopathic Hospital in October 1943. The second was established on December 3, 1924, at St. John's Hospital, Lowell, and was closed in 1927. It was reopened at the School Clinic Building on January 22, 1932, and was moved to Lowell General Hospital in 1933. The third was opened in December 1924 at the Town Hall, Reading, and closed on September 30, 1939. The fourth was opened on March 12, 1925 at the Beverly Health Center and was transferred to the Danvers State Hospital on April 13, 1932.

†It was opened on October 7, 1926, at the Quincy Dispensary, was conducted at the Woodward School from 1931 to 1943, and has been at the Children's Health Center since 1943.

Boston, and was well patronized by school principals and nurses. Restrictions of transportation in 1943 necessitated the closing of this clinic in October, and its cases were referred to the Southard Clinic in Boston.

The years 1929, 1930, 1931 and 1932 were significant in the establishment of ten state-hospital clinics.* The Fall River Clinic was a general psychiatric clinic until 1940, when it became a child-guidance clinic. These clinics, with the exception of Quincy, have continued to function on a weekly or monthly basis. The Quincy Clinic undertook the treatment of court cases and adolescents who were above age for the clinic conducted by the division in Quincy. After February, 1943, services were rendered only on call from the court or schools, and treatment cases were referred to the Division Clinic, which had for some time been accepting adolescents as well as younger children.

It had been the ambition of the division to have clinical facilities accessible to all citizens of the Commonwealth, but up to that time services had concentrated in the more populous eastern section. In May and June, 1931, demonstration clinics were instituted in Northampton and Holyoke and, following the six-month demonstration period, they were transferred to the auspices of the Northampton State Hospital in December, 1931.

In the year 1932, the division reopened the clinic at Lowell. This was a new type of co-operative venture undertaken at the request of the school department, which felt the need of a special school survey and the instruction of teachers in the principles of mental hygiene. The clinic was later moved to the Lowell General Hospital, and has changed in character because of its association with the hospital and its less central location. At the time of this resumption of responsibility, the Danvers State Hospital took over from the division the well established clinic at Beverly. In October of the following year, the Danvers State Hospital opened a clinic at the Community Health Center in Newburyport.

The year 1933 rounded out ten years of service of the state child-guidance clinics,²⁰ and various trends were in evidence. The original intention of the division to turn over its demonstration clinics to state hospitals as psychiatric centers of their respective districts had been carried out in six instances, and the hospitals had initiated clinics of their own in eight communities. The division itself was conducting nine clinics, which were acquiring

an aspect of permanence. Five of these were so-called "community clinics," affiliated more closely with schools and social agencies than with medical centers. Advantages were apparent in each type. The community clinics had become a part of community life, and were influential in the education of teachers through school conferences and in the education of parents through mothers' clubs and parent-teacher associations. The emphasis was on the problems of the normal child. The social and economic level of the patients was somewhat higher than that in the clinics that were affiliated with hospitals. The latter had advantages of medical services whenever needed and had a somewhat larger proportion of serious cases. These clinics also furnished an opportunity for instruction of medical interns and student nurses in the recognition and treatment of neurotic symptoms.

This period saw the beginning of special services in the clinics, such as speech correction, remedial reading and occupational therapy.

During these first ten years, the division had registered 5043 cases, which furnished a basis for analysis and research. Special studies and published articles by clinic personnel had become a part of the campaign for mental health.

The pressure of applications for intake necessitated the formulation of selective criteria for acceptance of cases suitable for clinic therapy, but the fact that the service was free under state support placed the clinics under obligation to accept maximum loads. This condition produced in an aggravated form the same dilemma that beset the generously staffed demonstration clinics of the Commonwealth Fund²¹ — the question whether to give intensive therapy to a few or more generalized treatment to many. Psychoanalytic procedure was impossible under the circumstances and would have met with popular prejudice, in fact, it was indicated in only a few cases that could be referred to private agencies, such as the Judge Baker Foundation, the New England Home for Little Wanderers and the Psychiatric Clinic of the Massachusetts General Hospital. Psychiatrists trained under various schools of thought directed their efforts toward improving parental attitudes and modifying the personal problems of children. In some cases the mother needed therapy as much as the child, and the social workers began to undertake this responsibility under the direction of the psychiatrists. The year-by-year discussions of all these problems in reports and bulletins give a dramatic picture of a pioneering effort with successes and failures but always un-failing enthusiasm.²²

The last ten years, from 1933 to 1943, have constituted a period of stabilization rather than of expansion. The division had reached the financial saturation point and could establish new clinics only by closing its less effective ones. Some new state

*These were as follows: Quincy, November 1929, auspices of Medford State Hospital at Quincy School Annex (closed February 1945); Fall River, 1930, auspices of Taunton State Hospital at City Hall Annex; Norwood, 1930, auspices of Medford State Hospital at Norwood Hospital (closed June, 1935); Gardner, July 1930, auspices of Gardner State Hospital, at Gardner High School, Fitchburg, July, 1930, auspices of Gardner State Hospital at Academy Street School, Haverhill, January, 1931, auspices of Danvers State Hospital at Haverhill High School (closed February 1944); Lawrence, January 1931, auspices of Danvers State Hospital at International Institute, Gloucester, January 1932, auspices of Danvers State Hospital, at Hovey School (closed June 1934); Warwick, 1933, auspices of Gardner State Hospital, at Central School and Athol, October, 1933, auspices of Gardner State Hospital at Red Cross Headquarters.

hospital clinics were started* The Salem Clinic has made a valuable contribution, the Waltham Clinic was doing intensive and effective work when it was closed for lack of personnel, the Amherst and Greenfield clinics served a hitherto neglected area.

In 1938, the Springfield Clinic expanded into a full-time clinic with financial contribution from the Community Chest. The school department furnished excellent quarters, and a sponsoring group formed the Guidance Clinic Association, which has acted in the capacity of an advisory board of directors.

The chief innovation of the division was the establishment of a clinic in Brockton on September 30, 1938, in co-operation with the school department, which has provided housing and stenographic service. In October, 1939, it expanded to two sessions weekly and still has an extremely heavy case load, obviously needing more service. This clinic exemplifies the type of clinic that can be developed through an intelligent educational policy to reach children of all ages. The clinic offers special services for speech correction, remedial reading and occupational therapy. Special classes for superior children have been in operation in the school system, with close supervision from the clinic. Brockton has an effective group of social agencies that co-operate with the Guidance Clinic both in case work and in a community program for mental health.

The division opened trial clinics in Hamilton (1940-1941) and Marblehead (1940-1942), which were discontinued because of lack of referrals by the communities. The Barnstable Clinic, opened in September, 1942, is developing as a mental-hygiene center for southeastern Massachusetts and Cape Cod, holding four sessions monthly at the Hyannis Town Hall.

The Quincy Clinic, which is a school and community clinic, has outgrown its original setup. In January, 1943, it added a second weekly session, and in December, 1943, moved to quarters in the Child Health Center. Community interest has resulted in the formation of the Guidance Association, which has obtained supplementary financial support for enlarged services. The Guidance Association is a member of the Quincy Council of Social Agencies, which is extremely active and promotes efficient social work in the city.

The new Southard Clinic, opened in Boston in 1943, is a different type of clinic and contemplates an extension of service for which the division has been clamoring for ten years. This clinic is a consolidation of the children's work of the Out-Patient

Department of the Boston Psychopathic Hospital with three division clinics that were discontinued to provide personnel. It is housed at the Boston Psychopathic Hospital and has the advantage of access to the specialized facilities of the institution for the diagnosis and treatment of serious cases. A definite disadvantage is found in the objection of many parents to any contact with a mental hospital, especially one that is stigmatized with the prefix "psycho-." This troublesome problem could be met by the erection of a separate building that would furnish headquarters for the Division of Mental Hygiene and the Division of Mental Deficiency, and would have a ward for the observation and treatment of young psychotic patients. Massachusetts has lagged behind other states in its failure to provide for segregation of such patients, who at present must mingle in the wards of mental hospitals with adult patients, an environment that is extremely detrimental to recovery.²³

The changes that have taken place in the last ten years have been in the direction of stabilization and efficiency. On January 1, 1944, nearly 12,000 cases had been accepted by the division clinics (exclusive of Springfield and Worcester) for diagnosis and therapy. The pressure of quantity has caused emphasis to be laid on essentials, economy of effort and selectivity of service. Co-operative resources have been utilized with mutual benefit. Student training has kept social workers up to date in methods of social therapy and has provided the clinics with assistance in case work. Special services in speech and reading, as well as hobby classes, have enhanced the value of the clinics. The constructive aim of helping children to attain a normal emotional maturity has been contagious and inspiring.

Twenty years of experiment and demonstration could not have been carried out on so large a scale without state financing. This provided security, minimized the effect of incidental failures, allowed changes of location and exchanges of responsibility between hospitals and the division, and made possible a statewide program for mental health. The benefits of such assistance outweigh the burdens and restrictions that are implicit in a state-supported service.

Much credit for the success of the child-guidance movement must be attributed to the gifted and forward-looking psychiatrists who initiated it and carried it on.

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MEDICAL PROGRESS

MYCOTIC INFECTIONS*

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NUMEROUS medical problems have been created by sudden changes in the living habits of large groups of the population. Emigration to different localities, the influx of workers into industries with which they have had no previous contact and the grouping of thousands of men in camps, both in this country and abroad, have contributed to the shifting problems of health. Diseases heretofore restricted to or endemic in certain areas or peculiar to certain industries have appeared sporadically and at times with epidemic proportions in areas or industries where they had not previously been reported. It is now necessary, therefore, that the practicing physician constantly focus his attention on an increasing horizon of infectious diseases.

Among such diseases, the mycotic infections have gained great importance. Previous epidemics of so-called "athlete's foot" among civilian members of social, fraternal or athletic organizations, due to the widespread use of showers and swimming-pool facilities, have become overshadowed by the rate of infection and seriousness of this disease among the troops. Safiron¹ has reported fungus infection as one of the five diseases most frequently attacking the skin of fighting men, and estimates the incidence of infection in various groups to be as high as 40 to 90 per cent. Downing² has also reported on the increasing problem of fungus infections in various camps. According to Goldstein and Louie,³ alarming numbers of American troops have acquired coccidioidomycosis while training in endemic areas in this country where *Coccidioides immitis* is known to occur in the soil. On return to civilian life,

these patients will scatter to all sections of the country and will necessitate the inclusion of coccidioidomycosis in the differential diagnosis of pulmonary infections outside of areas where the disease is known to be endemic. From the few samples cited above, it can readily be seen that the medical profession must gain a better understanding of the prevention and control of fungus infections.

With the exception of a few endemic areas, the geographic distribution of fungus infections is worldwide. The distribution of such diseases depends in reality on their recognition alone, and their frequency of occurrence demands that they be considered in the differential diagnosis of any infection of the skin or internal organs. It is the purpose of this article to present a résumé of the field of medical mycology as an aid to those who are comparatively unfamiliar with the types of infection produced by fungi.

Fungus infections can be conveniently divided into four major categories namely, superficial mycoses, dermatomycoses, subcutaneous mycoses and systemic mycoses. These will now be considered.

SUPERFICIAL MYCOSES

Included in the category of superficial mycoses are a few fungus diseases caused by a heterogeneous group of organisms, considered to be saprophytic species but occasionally producing superficial lesions on the skin or hair.

Tinea versicolor

Tinea versicolor is the most superficial of all the fungus diseases, with subjective symptoms lacking or with slight pruritus, the lesions involving usually the trunk but occasionally the neck, face, axillae and arms. The disease is characterized by a yellowish or brownish macular eruption and is caused by

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Malassezia furfur Although cultures of this fungus have been obtained,^{4, 5} the clinical diagnosis is confirmed by a microscopic examination of potassium hydroxide preparations of the furfuraceous scales covering the colored areas. In such preparations the fungus appears as clusters of round, thick-walled, budding forms intermixed with branching mycelial fragments. Treatment is directed toward the removal of the infected scales by daily hot, soapy baths, followed by an application of a 20 per cent aqueous solution of sodium hyposulfite.

Erythrasma

Erythrasma is a somewhat chronic superficial fungus infection confined to the skin of the axillary, pubic or genitocrural areas. The disease is characterized by sharply circumscribed maculopapular lesions having a reddish-yellow to reddish-brown pigmentation with overlying furfuraceous scales that feel greasy. The causative fungus, *Actinomyces (Nocardia) minutissima*, has been cultured but, as with tinea versicolor, the clinical diagnosis is confirmed by a microscopic examination of potassium hydroxide preparations of material scraped from the lesions. Such preparations reveal short, delicate, branching filaments 1 micron in diameter that are consistent in size with those seen in species of *Actinomyces*. The treatment is the same as that described for tinea versicolor.

Trichomycosis

Trichomycosis is an infection of the axillary or pubic hairs without involvement of the surrounding skin. The disease is characterized by lusterless, brittle hair with yellow, red or black concretions extending for some distance or occurring as isolated nodules along the hair shaft, and is caused by *Actinomyces*. Chromogenic cocci mixed in the mucilaginous material composing the nodules are responsible for the red or black pigmentation of the colored varieties.⁶ Microscopic preparations in potassium hydroxide reveal numerous cocci mixed with short, branching, thin mycelial fragments. Effective treatment involves shaving the hair and daily treatment with 3 per cent sulfur ointment or application of a 1:1000 solution of mercury bichloride.

Piedra

Piedra, a disease of the hair of the head or face, is known to occur in two varieties — black piedra, confined to the tropics and caused by *Piedra hortae*,⁷ and white piedra, occurring in the tropics and also in Europe, caused by *Trichosporon beigeli*.⁸ The disease is characterized by black or light-colored, hard nodules adherent to the hair shaft. As in trichomycosis, the surrounding skin is not involved. Because of the nodules the hair feels gritty when pulled between the fingers. The nodules of the black variety are composed of a compact

mass of wide, closely septate, thick-walled filaments, among which are scattered asci containing eight fusiform ascospores. The nodules of the white variety are composed of wide, closely septate filaments that break up into rectangular elements, budding cells and cocci. Microscopically these nodules are quite different from those seen in trichomycosis. Treatment consisting of vigorous shampoos or shaving, followed by the application of a 1:2000 solution of mercury bichloride or a 3 per cent ammoniated mercury ointment is usually effective.

Otomycosis

Otomycosis is a troublesome disease of the ear canal from which a wide variety of fungi have repeatedly been isolated. The majority of these fungi are saprophytic species, and their role in the disease is not completely understood. The infection is characterized by an exudative inflammation of the ear canal, which may extend to the external ear. Epithelial debris forms somewhat large masses that may interfere with hearing. An extensive pruritus, more noticeable at night, usually accompanies the infection. Treatment is directed toward the removal of all debris and keeping the ear canal dry.⁹⁻¹¹ Drugs having a bactericidal action should be used as a paint; these include a 1 per cent aqueous solution of gentian violet, a 1 per cent aqueous solution of silver nitrate and a 1 per cent aqueous solution of brilliant green. The sulfonamides, especially sulfanilamide, used as a dusting powder have also been found extremely useful. It can be seen that the use of these drugs is aimed at a possible primary bacterial infection of the ear canal as the underlying cause of the disease. Careful observation must be maintained, because of the danger of sensitization to the sulfonamides.

DERMATOMYCOSSES

Fungus infections belonging to the category of dermatomycoses are also superficial diseases of the hair, skin or nails, but they are caused by a related group of fungi, the dermatophytes. This group includes the genera *Trichophyton*, with about twelve species, *Microsporum*, with three species, and *Epidermophyton*, with a single species.

Microscopical examination of the infected hair, skin or nails in a 10 to 40 per cent potassium hydroxide preparation is the best method of ensuring an accurate diagnosis of this type of infection. Several modifications of this technic are advocated for preserving specimens for teaching purposes.¹²⁻¹⁵ Wood's light (filtered ultraviolet light), which causes infected hairs to fluoresce, is a great aid in the diagnosis and management of ringworm infection of the scalp.¹⁶ Hairs that fluoresce under this light should be examined microscopically for the presence of fungi. Since successful treatment de-

ends on complete epilation of the infected hairs, the Wood's light serves as an important aid in discovery and ultimate eradication of these foci of infection

Such preparations as are described above confirm the clinical diagnosis of fungus infection, but they cannot be used for the identification of the invading fungus. Trichophyton, Microsporum and Epidermophyton are similar in appearance when seen in potassium hydroxide preparations of infected skin or nails. Infected hair, however, usually reveals a definite mode of invasion by the genera Trichophyton and Microsporum. Since growth outside or within the hair shaft, or both, serves only as a generic character, it is necessary to culture the infected material to determine the species. It can be therefore seen that a complete identification of the invading fungus in all cases, whether the hair, skin or nails are affected, is possible only by obtaining cultures.

Such cultures are best secured by inoculating Sabouraud's glucose agar slants with several pieces of the infected material. When growth becomes established — in two to three weeks — preparations of the cultures in lactophenol cotton blue for microscopic examination reveal structures that allow their identification. The most useful structures for this purpose are the spore types and accessory organs.¹⁶⁻¹⁸

The genus Microsporum is characterized by numerous large, fusiform (spindle-shaped) macroconidia (fuseaux) and relatively few small, single-celled microconidia (aleuriospores). Whereas the species *M. canis* and *M. gypseum* produce macroconidia in abundance, *M. audouinii* produces abortive types of macroconidia or none at all. In culturing these species on rice medium these differences become apparent.¹⁹

The genus Trichophyton is characterized by a scarcity of clavate (club-shaped) macroconidia and numerous small, single-celled microconidia produced in grapelike clusters or singly along the hyphae. The macroscopic appearance of the cultures also serves to identify the species Trichophyton. The type of growth — powdery, cottony, smooth or waxy — the configuration and the pigmentation allow these fungi to be identified as *T. rubrum*, *T. rosaceum*, *T. gypseum*, *T. crateriform* or *T. faviform*. These species are not numerous, but can usually be identified only by those familiar with them.

Identification of the single species of the genus Epidermophyton, *E. floccosum*, presents no difficulty. The fungus grows on Sabouraud's medium as a powdery, sulfur-colored fungus and produces clusters or groups of short, stubby, few-celled, club-shaped macroconidia. No microconidia are produced by this fungus in culture. As the growth becomes older the culture reveals numerous chlamydospores.

The dermatomycoses show a wide variety of

clinical types, depending somewhat on the location of the infection on the body and the type of fungus causing the infection. It is not possible, however, constantly to associate the same fungus with a particular type of lesion, that is, favus may be caused by *T. (Achorion) schoenleinii*, *T. (Achorion) violaceum*²⁰ or *M. (Achorion) gypseum*.²¹ Whereas distinct clinical types of infection are recognized, the etiologic agent can be identified only by culture.

Tinea Pedis

This infection is known as "athlete's foot," dermatophytosis, epidermophytosis and so forth, but is probably better designated as tinea pedis. It is the most frequent of all the fungus infections, and the one causing the greatest concern among the armed forces. A simplification of the clinical types of this infection includes the acute, subacute and chronic forms caused by species of Trichophyton and by *Epidermophyton floccosum*.

The acute infection is characterized by vesicular or vesiculopustular eczematoid lesions, which usually begin between the toes but spread rapidly over the feet or along the soles. The vesicles contain a clear serous fluid until secondary pyogenic infection has taken place. This secondary infection produces ulcerating lesions, which spread rapidly. The foot becomes edematous and painful, with a rapidly developing cellulitis, lymphangitis or lymphadenitis. During this phase systemic reactions may occur.

Vigorous treatment of the acute infection must be avoided until the symptoms have disappeared. Compresses of a saturated solution of boric acid, a 1:4000 solution of potassium permanganate or physiologic saline solution should be used constantly, with the patient in bed and the feet elevated. If the secondary pyogenic infection is caused by a staphylococcus or streptococcus, penicillin should be used. After the acuteness of the lesions has subsided, half-strength Whitfield's ointment or 10 per cent sodium propionate in a water-soluble base may be employed. Treatment should be continued for a week or two after the lesions have healed. A dusting powder should be used as a prophylactic.

The subacute infection is characterized by vesicles or vesicopustules of a spreading type, usually starting between the toes. Absence of a superimposed secondary pyogenic infection of the vesicles permits this type of infection to be managed more easily than otherwise. A lymphangitis or lymphadenitis may result, however, and conservative treatment by compressing should precede the use of keratolytics or fungicidal agents. The same kind of treatment as used in the acute infection is often necessary.

The chronic infection is characterized by fissuring between the toes and an accumulation of soggy dead tissue. Hyperhidrosis is usually present, and treatment must be directed toward controlling this condition. Ointments containing a keratolytic (half-strength Whitfield's ointment) can be used to re-

move the dead and infected tissue. Care should be taken to avoid irritating the skin, which may result in an acute flareup. Dusting powders employed as a prophylactic and also as a drying agent are beneficial.

That there is no specific method of treating cases of *tinea pedis* has been clearly demonstrated by the recent appeals of the medical services of the Army and Navy for help in combating this type of infection. This fact has brought about in vitro studies of new drugs that might prove to be more effective fungicidal or fungistatic agents²²⁻²⁴. Concise outlines of management have also been published, as well as data concerning the clinical trial of new drugs. Peck and Schwartz²⁵ have outlined a plan of treatment and have given numerous prescriptions that prove helpful in various types of infection. Crittenden and Joiner²⁶ have used cotton hose impregnated with copper sulfate or copper acetate. Bograd²⁷ has used ethyl chloride as a spray to cover infected areas. Wallace et al²⁸ have used a chlorophyl ointment. Recently Keeney and Broyles²⁹ have reported on the use of propionate acid and the higher fatty acids as beneficial therapeutic and prophylactic agents. No standard method of treatment has, however, resulted from these studies.

Recurrence of infection may result from a previous inadequate treatment of the infected foci or from reinoculation through contaminated contacts. Prevention must therefore include a thorough search for remaining foci of infection and adequate instructions to the patient concerning how contacts may best be avoided.

Shoes, socks, stockings and clothing may be sterilized by formaldehyde vapor. The articles should be placed in a container with a tight-fitting cover, along with old rags or crumpled newspapers soaked with the formaldehyde. The fumes should kill all fungus material in a period of twenty-four hours. These articles are then well aired to avoid a subsequent dermatitis. Cotton socks may be boiled for twenty minutes or soaked in a 1 per cent solution of liquor cresolis saponatus *U S P* overnight and washed in cold water. Women's stockings may be soaked in 90 per cent grain alcohol for twenty-four hours.

A dusting powder (2 per cent salicylic acid, 3 per cent zinc stearate, 6 per cent boric acid, 10 per cent starch and 79 per cent powdered talc) should be used in the shoes and socks and dusted on the feet. Also, the feet may be painted once or twice a week with a sodium propionate lotion, containing 8.2 per cent sodium propionate, 1.2 per cent propionic acid and 10 per cent N-propyl alcohol. The feet should be kept clean, clean socks should be worn every day, and if excessive perspiration is serious, a drying agent (aluminum acetate) should be occasionally used.

The patient should be warned about possible places of contamination, that is, shower baths or

bathroom floors. Newspapers or similar material that is easily disposed of should be used on the bathroom floor instead of mats. The tub should be thoroughly cleaned and dried after use. A rubber mat for the shower floor should be washed and placed in the sun to dry. Slip-on rubber sandals can be worn in the showers, and to and from them in gymnasiums and swimming pools. Too much reliance should not be placed on the foot baths to be found in these places. Often they are hurriedly used, become diluted or contaminated with organic materials and are not frequently freshened. All these factors, together with the doubtful fungicidal activity of the various types of foot baths, advocate the destruction of the value of this type of prophylactic measure.

Tinea Corporis

Fungus infections of the glabrous skin, which have been designated as *tinea glabrosa*, *tinea circinata*, ringworm of the smooth skin and so forth, are caused by species of *Microsporum* and *Trichophyton*. The lesions resulting from this type of infection vary greatly, and the clinical diagnosis should be confirmed by laboratory examinations of material obtained from the lesions and by culture.

Infections on the glabrous skin vary from extremely superficial scaly annular lesions to an erythematous squamous or deep granulomatous type. The usual lesion begins as a red papule, which spreads peripherally while healing in the center. The erythematous border has many minute vesicles and pustules, with some crusting. This type of circular lesion with reddened active border and healing scaly center is typical of ringworm, or *tinea circinata*, of the skin.

If the lesion begins as a vesicle or group of vesicles that break down and form a rather large crusted area with peripheral vesiculation but no central healing, the lesion is usually referred to as the eczematous type. Such lesions may be single or multiple, coalescing to form large configurations.

Suppurative, deep, granulomatous lesions begin as red, indurated nodules centered around perifollicular abscesses. Discharge of pus and ulceration of the skin are indications of a severe infection.

The type of infecting organism cannot always be determined by the clinical appearance of the lesions. It is now well known that a single fungus can produce different types of lesions and that different fungi can produce similar lesions. In some cases, however, certain species are somewhat consistent in the type of lesion that they produce. The configuration of the lesions found in *tinea imbricata* of the tropics and of South and Central America is characteristic of an infection produced by *T. concentricum*. Also, the cuplike structures (scutula) on the scalp and glabrous skin in *tinea favosa* are somewhat characteristic of invasion by *T. (Achorion) schoenleinii*. It must be remembered, however, that

both *M. (Achorion) gypseum*²¹ and *T. (Achorion) violaceum*²⁰ have also been isolated from typical avus lesions. It has been pointed out that *T. rubrum* (*purpureum*) also produces a somewhat specific reaction.²⁰

The only reliable means of determining the type of invading fungus is culture and identification of the resulting growth. Material for culture is obtained from the erythematous border of the lesions by scraping or by curetting the tops of vesicles. This material should be examined microscopically in potassium hydroxide and cultured on Sabouraud's glucose agar slants. Since an accurate prognosis depends on the type of infecting organism — that is, *T. rubrum* and *T. schoenleinii* produce stubborn, resistant infections, — cultures should be obtained and identified whenever possible.

Treatment of tinea corporis is not difficult unless the invading fungus happens to be either of the two mentioned above. Even in these cases, successful treatment is possible, but it must be prolonged and more intensive.

Ointments (5 per cent ammoniated mercury, 3 per cent salicylic acid and 5 per cent ammoniated mercury or 3 per cent precipitate sulfur and 3 per cent salicylic acid) or a 3.5 per cent tincture of iodine should be applied twice daily. When the vesicular lesions become crusted, it is necessary to remove the crusts and thoroughly rub in the ointment. Cure should be effective in two weeks.

Lesions on the glabrous skin that simulate in every detail the clinical appearance of active fungus infections occasionally fail to heal after appropriate treatment. Serious consideration should be given to such cases to establish whether fungi are locally present in the lesions or whether the lesions are the result of hypersensitivity, that is, dermatophytids or secondary eruptions occurring in a sensitized person. These dermatophytids may occur anywhere, but are found particularly on the palmar aspects of the hands as a result of a hematogenous spread of a fungus or its products from a primary focus of infection elsewhere on the body. These primary foci are usually confined to the feet,³¹ are unnoticed by the patient, and sometimes are discovered only after a thorough investigation. Occasionally, too vigorous treatment of tinea pedis causes a generalized dermatophytide reaction. It is therefore necessary to examine microscopically material from lesions of the glabrous skin to establish the presence or absence of fungi. When fungi are not seen in such material, the primary focus of infection must be found and treated. In such cases the dermatophytide reaction subsides as the primary focus heals.

Tinea Cruris

Tinea cruris, or ringworm infection of the groin, also known as tinea inguinale, eczema marginatum, jockey itch, dhotie itch and so forth, is a circum-

scribed, well demarcated infection of the crural region usually caused by *Epidermophyton floccosum* and occasionally by species of *Trichophyton*.

This infection was known to Harz²² in 1871, at which time he cultured *E. floccosum* from it. The lesions are usually bilateral, elevated, papular, scaly, red areas with a sharply demarcated border of vesicopustules. Although the inner thighs are the areas usually involved, the infection may spread to the sacrum or involve the pubic areas. The disease is more frequent in males than in females but is often seen in the latter. Epidemics have been reported³² in regions where people were living closely together under crowded conditions.

Treatment with ointments (half-strength Whitfield's ointment and 3 per cent precipitated sulfur and 3 per cent salicylic acid in petrolatum) or with Castellani's paint is usually effective in two weeks. Occasional stubborn cases necessitate prolonged treatment. Careful laundering of wearing apparel is important to avoid reinfection.

Tinea Unguium

Ringworm of the nails or onychomycosis of the hands or feet usually accompanies tinea pedis or infection elsewhere on the body, but can occur as the only presenting lesion. This disease is caused by species of *Trichophyton*, *Epidermophyton floccosum* and *Candida (Monilia) albicans*.

Nails infected by the dermatophytes show yellowish discoloration, and become lusterless, friable and thickened, often with great amounts of material beneath the nail. Paronychia is not an accompanying symptom. Material should be scraped from the discolored or friable areas and from beneath the nail for microscopic examination and culture. The fungi appear as branching filaments when the infection is caused by the skin fungi.

Nails infected with *C. albicans* have an accompanying paronychia. The nails become thickened, grooved and brownish but remain translucent and do not become brittle. This fungus appears as small, budding, egg-shaped cells in the infected material.

Treatment of nails infected with dermatophytes consists of filing or scraping the infected portions of the nail as thoroughly as possible. The scraped nail may be painted with chrysarobin (20 per cent in chloroform), taking care to avoid contact with the skin, rubbed with sulfur salicylic acid ointment (10 per cent each of precipitated sulfur and salicylic acid in equal parts of lanolin and rose water ointment) or painted with 1 per cent iodine in alcohol. Before each medication the old material should be scraped off the nail. Surgical evulsion of a nail is sometimes necessary. Nails infected with *C. albicans* should also be scraped and the nails soaked in a 1:4000 aqueous solution of potassium permanganate three times daily, followed by a paint containing 1 per cent gentian violet or an ointment

containing 5 per cent ammoniated mercury. Whether infection is caused by the dermatophytes or by *C. albicans*, the treatment is prolonged and may last for months before a cure can be expected.

Tinea Barbae

Ringworm of the beard, known as sycosis parastitica, tinea sycosis and so forth, is a stubborn, chronic fungus infection of the bearded region of the face and neck, with rare involvement of the upper lip, caused by species of *Trichophyton* and *Microsporum*.

Two types of infection may be encountered in the bearded area: a superficial dry lesion with a central scaly area and an active vesiculopustular periphery or areas of perifollicular pustules with lusterless hairs progressing to red, deep-seated nodules and boggy masses with adenitis of the regional lymph nodes. Such areas are undermined, and extrusion of purulent material occurs, with resulting crust formation. The hairs are brittle and easily epilated. Involvement of the upper lip has been reported,^{34, 35} but is rare. Microscopical examination of material from the lesions is the only means of determining the fungus nature of the infection.

The patient should be instructed in the sterilization of his shaving articles. Manual epilation of all infected hairs is necessary for complete cure. In some cases x-ray epilation may be necessary. Compresses of hot boric acid solution, a 1:4000 aqueous solution of potassium permanganate or Vlemminckx's solution, diluted 1:10, followed by a 5 per cent ammoniated mercury ointment rubbed well into the skin, should prove successful.

Tinea Capitis

Ringworm infection of the scalp, tinea capitis, is essentially a disease of childhood, with a variety of clinical appearances, and is caused by species of *Trichophyton* and *Microsporum*.

The appearance of lesions on the scalp caused by the dermatophytes varies according to the type of infecting fungus and the response of the patient. Some species of *Microsporum* and *Trichophyton* cause an inflammatory reaction leading to large, boggy, tumorlike masses (kerion). In such areas, the infected hairs are dislodged easily and there is a tendency to spontaneous cure. Other species do not evoke an inflammatory reaction and are more difficult to manage and treat.

Infection by species of *Microsporum* usually results in a few scaly, gray patches in which the hairs are broken off 3 to 4 mm from the surface of the scalp. Microscopically, the hairs are seen to be surrounded by a sheath of angular spores arranged in a mosaic pattern.

Infection by species of *Trichophyton* results in a variety of lesions depending on the particular species involved. Infection by *Trichophyton schoenleinii*, the usual cause of favus, is characterized by the

formation about the hair follicle of a yellow crust with a depressed center, giving a cuplike appearance. Such cups, or scutula, contain mycelium and cellular debris and are pierced by the hairs. Microscopically, the hairs are seen to be of the endothrix type, with invasion of the fungus inside the hair shaft. A seborrheic eczema type of lesion with diffuse superficial scaling may also be caused by this fungus. Examination of the hairs is necessary for a differential diagnosis. Infection by other endothrix species (*T. violaceum* and *T. acuminatum*) may be characterized by small, scattered, scaly crusts over the scalp with the hairs broken off at the surface. The follicles protrude and have a black center (black-dot ringworm), or the hairs may not be broken off but be folded in the scales of the crusts forming the lesion (*T. tonsurans*).

Species of *Trichophyton* belonging to the ectothrix group, such as *T. mentagrophytes* (*gypseum*), in which the fungus is seen outside and surrounding the hair shaft as parallel rows of spores, produce inflammatory and suppurative lesions leading to kerion formation. This type of infection may be mistaken for pyoderma, and the only satisfactory diagnosis is that based on a microscopic examination of the hair. Since an inflammatory reaction may develop a sensitivity of the skin, patients with kerion of the scalp may exhibit rashes on the trunk or extremities. This type of reaction has been known for some time^{31, 36} and, as mentioned previously under tinea pedis, is the result of a hematogenous spread of the fungus or its products from a primary focus of infection. Such lesions, dermatophytides, do not contain the fungus, are an allergic manifestation and disappear as the primary focus heals.

Treatment of tinea capitis must be guided by the type of fungus causing the infection. *M. audouinii*, *T. schoenleinii*, *T. violaceum* and *T. tonsurans* cause resistant infections that are difficult to manage. The lesions of *M. audouinii*, however, tend to heal spontaneously as puberty is reached. *T. schoenleinii* and *T. violaceum* produce lesions that do not heal spontaneously at puberty but remain through the adult years. On the other hand, *M. canis*, *M. gypseum* and *T. mentagrophytes* cause lesions that may heal spontaneously at any time, especially if an inflammatory reaction is induced. It is therefore necessary to obtain cultures and identify the fungus from each case for a proper evaluation of prognosis and treatment.

Treatment is directed toward the removal of all infected hairs. Wood's light is invaluable as an aid in detecting these hairs and should be constantly used during the management of the disease. Hairs infected with the following fungi fluoresce under this light: *M. audouinii*, *M. gypseum*, *M. canis*, *T. schoenleinii*, *T. violaceum*, *T. tonsurans* and *T. mentagrophytes*.

A conservative type of treatment may be used when the infection is one that is likely to heal sponte-

ineously. An ointment containing 5 per cent ammoniated mercury or 10 per cent sulfur ointment with iodine crystals should be rubbed well into the scalp. Daily shampooing, with a stiff brushing, removes the loosened infected hairs. The shampoo should be followed each time with the ointment.

Treatment of the infection, which is likely to remain until puberty or be carried over into adulthood, demands better methods of epilation. Manual epilation with forceps is practical only when small areas of the scalp are infected, and should be repeated every four days. For larger areas, the hair should be clipped close and adhesive plaster applied tightly and pulled off to remove the loosened hairs. An ointment of 10 per cent ammoniated mercury rubbed into the scalp will prevent infection of healthy areas, and an adhesive-plaster patch over the infected areas will prevent the loosened hairs from falling out to cause reinfection or epidemics. Roentgen-ray epilation may be desirable in certain cases, but should be done only by one fully experienced in its use.⁴⁷ Thallium acetate should be used only when contraindications are lacking and the patient is hospitalized.

Estrogenic substances³⁸ in the treatment of tinea capitis caused by *M. audouinii* and trichophyton³⁹ as a therapeutic agent for ringworm of the scalp have not as yet given satisfactory results.¹⁶

SUBCUTANEOUS MYCOSES

Infections of the subcutaneous tissues are caused by a wide variety of fungi, which produce lesions simulating those of syphilis, tuberculosis, and pyogenic infections as well as granulomas and neoplasms. Three of the frequent types of such infections will be discussed below.

Chromoblastomycosis

This disease, often referred to as chromomycosis or verrucous dermatitis, caused by *Hormodendrum pedrosoi*, *H. compactum* and *Phialophora verrucosa* and thought previously to be of rare occurrence in the United States, has gained widespread interest, owing not only to the increased number of cases encountered in this country but also to the atypical forms of the disease that have been reported.

Chromoblastomycosis is a disease, usually of the lower extremities, producing unilateral lesions of warty papillomatous vegetations (verrucous dermatitis). Fibrosis and blocking of the lymphatics produce an elephantiasis, ulceration and secondary infection may occur. There is no systemic involvement or involvement of the bones and the general health remains good.

Recent reports in the literature,⁴⁰⁻⁴² however, have referred to the protean nature of the infection and to the difficulty of making a clinical diagnosis before a long-standing infection brings about the typical verrucous appearance of the lesion. Also, the diagnosis may not be readily apparent if lesions occur

in areas of the body other than on the feet, such as, the hand,⁴³⁻⁴⁶ the arm,⁴⁷⁻⁴⁹ the face,^{40, 50} the neck⁵¹ and the buttock.⁵²

Diagnosis should be made by laboratory examination of pus, crusts or biopsy sections in which the unmistakable dark-brown splitting bodies of the fungus are found. Since the different fungi (*Hormodendrum pedrosoi*, *H. compactum* and *Phialophora verrucosa*) known to produce this disease appear identical in tissue, cultures on Sabouraud's glucose agar should be made to determine exactly the fungus responsible for a given case.

There is no general agreement on the nomenclature for these fungi.^{42, 53, 54} The various spore types produced by the single species *H. pedrosoi* in culture have allowed this fungus to be placed in numerous genera according to the emphasis placed on a given spore type.

Treatment of the extensive lesion is unsatisfactory. Potassium iodide, with and without x-ray therapy, and iontophoresis⁴⁹ have been used. Early lesions, if diagnosed, should be removed by excision or destroyed by electrocoagulation.

Maduromycosis

This disease, also referred to as Madura foot or mycetoma, is produced by the greatest assortment of heterogeneous fungi. In spite of this, however, it is generally agreed that the disease is a clinical entity, and its pathology remains fairly constant regardless of the type of fungus causing the infection.

Deep-seated chronic infections of the subcutaneous tissues of the feet cause, over long periods of time, swelling and clubbing of the involved member, resulting in marked deformity. This may be accompanied by destruction of the small bones of the foot and extensive fusion of these structures. There are no systemic reactions and little pain, and the foot can be used with slight discomfort.

Scattered over the deformed foot may be seen numerous abscesses, which rupture, drain and develop into fistulas. The serosanguineous fluid from such fistulas contains the macroscopic colored grains (white, black, yellow or red) that are diagnostic when seen microscopically. Such grains are composed of a mass of broad, septate, branching hyphae containing numerous chlamydospores. The width of the hyphae and the presence of chlamydospores differentiate these grains from the granules seen in actinomycosis. In the latter disease, the granules are made up of a mass of delicate hyphae, 1 micron in diameter, which usually terminate in club-shaped swellings at the periphery of the granule.

These differences early led to the classification of mycetoma into two categories by Chalmers and Archibald⁵⁵ actinomycotic mycetoma, caused by species of Actinomycetes and maduromycosis, caused by species of higher fungi and molds. Although this classification is adhered to by many investigators,

some retain a single term, maduromycosis, since the disease is clinically and pathologically an entity regardless of the particular fungus found to be associated with a given infection

Recently, however, Symmers and Sporer⁵⁶ have reported an infection of the hand in a native American in which new histologic features were observed. Whether these findings were the result of an infection by the particular fungus responsible for their case and do not occur in infections by other hyphomycetes can be determined only by a comparative study of tissues from many cases. At the present time these authors believe that maduromycosis is a distinct disease quite different clinically, pathologically and mycologically from any other disease, particularly actinomycosis.

The various fungi that have been isolated from mycetoma are listed by Conant et al.⁵⁷ Of the 38 cases reported from the United States, only 11 can be classified as maduromycosis as proved by culture. The following fungi have been isolated: *Allescheria boydii*,⁵⁸ *Madurella americana*,⁵⁹ *M. ikedai*,⁶⁰ *M. lackawana*,⁶¹ *Aspergillus nidulans*,⁶² *Monosporium apiospermum*,^{57, 63-66} and *Torula* (?) *jeanselmei*.⁵⁶ Emmons⁶⁷ has shown that two of these fungi, *Allescheria boydii* and *M. apiospermum*, are but different phases (an ascomycetous and the imperfect stage) of a single organism.

Treatment of maduromycosis caused by the higher fungi is not satisfactory. Secondary infections by pyogenic organisms may be controlled by using sulfonamides or penicillin. The usual case, however, requires amputation.

Sporotrichosis

Whereas other fungus infections involving primarily the subcutaneous tissues are caused by a group of fungi, sporotrichosis is caused by the single organism *Sporotrichum schenckii*. Although this fungus can and does infect the entire body, producing widespread disseminated lesions, the disease is discussed among those involving the subcutaneous tissues because it is this type of infection that is encountered more frequently in the United States.

The initial lesion follows an abrasion of the skin, usually on the fingers or hands, and presents itself as a superficial necrotic ulcer that fails to heal under ordinary treatment. Lymphatics draining the area show a marked inflammation and develop multiple deep nodular subcutaneous abscesses, which usually terminate in ulceration. The intervening lymphatic vessels become thickened and cord-like in consistency. The regional lymph nodes are not involved, and the patient presents few, if any, systemic symptoms.

A clinical diagnosis of sporotrichosis is confirmed by obtaining cultures of *S. schenckii* from the ulcers or unruptured subcutaneous nodules.

This so-called "localized" lymphatic sporotrichosis is the usual type of case encountered in the United

States. Moore and Kile,⁶⁸ Forbus⁶⁹ and Singer⁷¹ have reported some of the rare disseminated cases of the disease. In Europe, however, extensive infections are the rule and any organ of the body may be affected. De Beurmann and Gougerot⁷¹ classify the clinical types as lymphatic, disseminated, epidermal, mucosal, skeletal and visceral.

Sporotrichosis may be acquired from plants or infected animals. Foerster⁷² reported cases following injury by barberry thorns and considered the disease to be an occupational hazard among farmers and horticulturists. Meyer⁷⁴ has reported infections in man following the bites of horses, dogs, hens and parrots. Anderson and Spector⁷⁶ have reported an associated sporotrichosis with rat-bite fever.

Treatment of sporotrichosis is most satisfactory with potassium iodide. Of all the fungus infections, sporotrichosis is the only one that responds specifically to this drug. Occasionally, however, an exceptional case may not respond to iodides.^{76, 77} In such cases sulfonamides may be used either orally⁷⁸ or locally.⁷⁹

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31311

PRESENTATION OF CASE

A thirteen-week-old male infant was admitted to the hospital because of vomiting of blood-streaked material.

The child was the first of twins born seven weeks prematurely. This was the fifth pregnancy of the mother, and labor was short and easy. The birth weight was 3 pounds, 1 ounce. The other twin weighed 2 pounds. Both children vomited frequently, and the other child died after one week. The patient was fed human milk by gavage many times while in the hospital. In eight weeks the child was discharged, weighing 5 pounds. On the day he arrived home he vomited white curds with some dark-brown streaks. During the ensuing five weeks he vomited after almost every feeding, with frequent dark-brown streaks and material among the curds. Three days before admission, just before his evening feeding, the baby vomited a large quantity of dark-brown shiny material. He vomited again after the feeding, and the vomitus was streaked with a dark-brown substance. On the day before admission the baby was taken to a physician. While in the doctor's office the baby vomited. The vomitus, which appeared like that of the past few days, was tested by the physician and found to contain blood. On the evening before admission the baby again vomited large amounts of dark-brown material mixed with curds. While at home, he had been on a formula consisting of 16 ounces of milk and 3 tablespoonfuls of Karo, with no fruit juice or vitamin supplement. During these five weeks he had gained only 7 ounces. The mother stated that she was always careful to "bubble" the child, but despite this he would vomit about ten minutes after each feeding. The mother states that he did not vomit the entire meal. He usually had five bowel movements a day, the stools varying from yellowish and formed to greenish and liquid.

Physical examination revealed a severely undernourished and underdeveloped infant, measuring 47.5 cm. and weighing 5 pounds, 8 ounces. He ap-

peared vigorous, with a lusty cry, and seemed in no distress and fairly well hydrated. There were no skin lesions. The fontanelles were open and flat. Examination of the heart and lungs was normal. The abdomen was normal. No peristaltic waves were seen with feeding, and no masses were felt.

The temperature was normal, the pulse 110, and the respirations 40.

Examination of the blood showed a red-cell count of 3,800,000 with 8.6 gm. of hemoglobin, and a white-cell count of 16,300, with 66 neutrophils, 23 lymphocytes, 9 monocytes and 2 eosinophils. The urine was negative. The bleeding time was 6 minutes, and the clotting time 4 minutes, clot retraction was good. A tourniquet test was negative. The prothrombin time was 20 seconds (normal, 18 to 20 seconds). Vomitus and stool examinations were strongly positive for blood. A Hinton test was negative. A skin tuberculin test in a dilution of 1:100 was negative. The blood was Rh negative. The serum protein was 5.1 gm. per 100 cc. The nonprotein nitrogen, chloride, sodium and phosphorus were normal. The alkaline phosphatase was 13.7 units per 100 cc. A cephalin flocculation test was negative.

X-ray examination of the chest showed an area of increased density, apparently collapse, in the right upper lung field. There was extensive increased density in the left upper and right lower lung fields. Films of the long bones of the forearm showed no definite abnormality. A barium swallow showed the esophagus to be rather wide, but there was no demonstrable fistula between it and the trachea and no constant defects were seen. The stomach was likewise dilated, and in the distal portion there appeared a rather constant filling defect in the region of the lesser curvature. In the proximal portion of the second part of the duodenum there was a rather constant narrowing. During the examination, the barium and food content of the stomach frequently regurgitated into the esophagus. A twenty-four-hour film showed that practically all barium had passed through the duodenum.

Because of the lesion in the lungs the child was started on penicillin, 6000 units every three hours. An exploratory laparotomy was done about two weeks after admission. No duodenal obstruction or any other abnormality was found. The child withstood the operation well but continued to vomit his feedings and large amounts of coffee-ground material. He was then taken off feedings by mouth and maintained parenterally. When feedings by mouth were resumed, he again started to vomit. Attempts to stop the vomiting with sedation and with atropine were unsuccessful. Thickening of the formula was likewise not helpful. The child went downhill in spite of supportive treatment and died two weeks after the operation.

DIFFERENTIAL DIAGNOSIS

DR. SIDNEY FARBER * The patient was one of twins. The sibling weighing 2 pounds and dying after one week, with a story of vomiting, might have died because of a congenital malformation. Possibly there was infection or hemorrhage. Hemorrhage in general is the most frequent single finding in premature babies who die within ten days after birth. The fact that both babies vomited may have been merely coincidental or possibly both were suffering from the same type of malformation. Savage feeding of premature babies is frequently a necessity and saves many lives. It may be the cause of ulceration of the esophagus, however, particularly when the feedings are performed by inexperienced people. Such ulceration may form the starting point for infection, which may end in bacteremia.

We might expect that this baby had evidence of curvy and rickets in addition to other disturbances of calcification of the bones characteristic of premature babies of this size. The baby's length at thirteen weeks of age was several centimeters less than that of a full-term normal baby at birth, and the weight was roughly one third to one half of the normal weight for a full-term baby of the same age.

The findings in the differential count are of interest but give no specific information concerning a definite diagnosis. I am not familiar with the type of tourniquet test performed on premature babies of this size, but apparently there was no unusual bleeding into the skin after this was done. The tuberculin test is usually done in a dilution of 1:1000, which is not sufficient to exclude tuberculosis. Someone must have thought of that diagnosis perhaps a tuberculous ulcer of the stomach, and a test in a dilution of 1:100 was carried out before this lead was abandoned. Determination of the Rh factor is part of every routine study of the blood. I am not familiar with any disease associated with Rh blood incompatibility that would manifest itself at the age of eight to thirteen weeks, with bleeding for so many weeks thereafter. The serum protein was below normal but within the range of premature babies of this size. Occasionally with bleeding in the gastrointestinal tract the nonprotein nitrogen is increased, but here it was within normal range.

I am not familiar with the value of information derived from a cephalin flocculation test in a premature baby of this age. Let us take it as it is stated—negative. I do not believe that excludes liver disease.

From the x-ray examination we may exclude obvious rickets, scurvy and any of the important abnormalities of the skeleton associated with prematurity. The report states that the esophagus was wide, it does not say "dilated." It certainly appears to be wider than normal on these films.

*Assistant professor of pathology Harvard Medical School pathologist, Children's Hospital Boston

I assume that the fistula which was looked for was one that might have been acquired secondary to the aspiration of a foreign body, a pin or something of that kind, a congenital tracheoesophageal fistula would not be thought of at this age. May we hear from the roentgenologist?

DR. MILFORD D. SCHULZ The esophagus is wide, and there are numerous defects within it, which appear to be gas bubbles. I do not see the defect along the lesser curvature of the stomach, mentioned in the protocol. The fluoroscopist must have seen it, unless it is this area on the spot films. Again the constant narrowing of the duodenum apparently was a fluoroscopic observation.

DR. FARBER You see no evidence of duplication of the esophagus or any mass pressing against it?

DR. SCHULZ No, nor of barium in the lungs. The films of the chest are essentially as mentioned in the protocol, and I do not believe that I can add anything.

DR. FARBER I am afraid that I can say nothing more concerning the films. We have to rely on the evidence from fluoroscopy that there was a true filling defect in the lesser curvature and duodenum since these findings are not present on the films. The consolidation in the right upper lung field, with a story of vomiting, is perhaps best explained by aspiration of vomitus, which often occurs in a premature baby, but before seeing the x-ray films I suspected that a mass attached to the esophagus compressing the lung might have been present.

It must have been decided at the time of exploration that the story was not simply that of vomiting or blood streaking associated with any of the ordinary diseases of the hematopoietic system. There must have been a suspicion that an organic lesion would be found.

We have a problem here, then, which is unusual—that of vomiting of five weeks' duration before admission and of four weeks' duration after admission, with blood streaking of the vomitus in a small prematurely born infant who had gained little weight since birth. There are several possibilities that should be considered before a definite diagnosis is attempted.

Foreign body, to take the least likely possibility, is fairly frequent in children between one and two years but is relatively rare in small babies of this size, unless some extraordinary accident occurs, such as the swallowing of a safety pin or something of that kind. Foreign bodies may cause definite ulceration, particularly if they are sharp. I recall a child who swallowed a piece of artificial denture immersed in nitric acid and developed a duodenal ulcer, which was cured surgically.

Next in line of possibility are a combination of defects associated with the pancreas and an ulcer of the duodenal surface. An annular pancreas causing constriction of the duodenum can give a picture

like that described, but it would not account for the filling defect in the lesser curvature. We would have to assume that there was an ulcer of the mucosa of the duodenum or stomach, or both, if we were to give one diagnosis. There are occasional cases of annular pancreas associated with malformation of the portal region, so that portal obstruction is caused and a Banti type of obstruction is produced, with esophageal varices or varices in the stomach. This combination of circumstances is a possible explanation. These diagnoses are unlikely.

Another remote possibility, which we have encountered, is a congenital Eck's fistula associated with portal obstruction and, again, esophageal varices to account for the bleeding. Adhesions associated with malformation of the portal system might have caused the duodenal obstruction. But we are left without an explanation for the defect in the stomach.

More probable are two explanations. The first is that he had duplication of the intestinal tract, probably in several locations. This may occur in one area, or there may be six or seven along the course of the intestinal tract. There is no evidence of duplication of the esophagus, nor evidence in these films of duplication of the stomach compressing the lesser curvature or the duodenum. The x-ray studies would have disclosed such duplication, had it been there. Without evidence, however, I can do no more than mention it. Duplication of the intestinal tract may cause constriction, and there may be hemorrhage over a long period of time because of interference to the blood supply of the duodenum or stomach by the duplication, which receives its blood supply from the same source as the adjacent bowel.

The second probable explanation, and perhaps the most logical one, would account for the bleeding, either a tumor or ulcer in the stomach or duodenum. Tumors of the gastrointestinal tract in infants and children are extraordinarily rare. It might be of interest to mention that Dr J. Hawkins¹ has found that tumors of the brain in children as compared with those in adults occur in a ratio of 1:8, tumors of the kidney and adrenal gland in a ratio of 1:14, and carcinoma of the stomach and duodenum in a ratio of 1:10,000. Thus, tumors of the stomach and duodenum are rare. The only tumor that I should like to mention is a hemangioendothelioma or hemangioma, which may infiltrate the wall of the stomach or duodenum and may be found in the lower portion of the esophagus. These can bleed regularly and can be responsible for this kind of blood-streaked vomitus.

Our problem here is to find a lesion that caused irritability of the stomach, because the stomach expelled food a few minutes after eating and also caused actual bleeding. The final possibility, therefore, is duodenal ulcer or a combination of duodenal and gastric ulcers. These are more frequent in infancy and childhood than is generally recognized. They may occur in the first or second part of the

duodenum or in the pyloric end of the stomach. We have to choose a lesion that not only caused vomiting and bleeding but could not be found at operation. The lesion likeliest to hide itself in a patient of this age is an ulcer or, probably in this case if we take the defect in the lesser curvature of the stomach seriously, two ulcers. Ulcers in young infants of this age are sometimes multiple. If these ulcers are small and are located in the first portion of the duodenum, on the posterior wall or on the medial surface, — the so-called "silent" area of the duodenum, — they may not be readily found at exploration and may be found only with some difficulty at autopsy, when the entire specimen is removed and careful dissection is made posteriorly. Such ulcers usually do not cause bleeding for so long a period of time as we have heard about here. This represents an unusual history for ulcer of the duodenum or of the stomach. In infants or children the story of bleeding is usually a very direct one and death occurs in most cases within twenty-four or forty-eight hours after the onset of hematemesis.

Either a hemangioma of the stomach or duodenum or an ulcer could have been present and yet not have been seen at operation. Therefore in order of probability my diagnoses are question of duodenal or gastric ulcer and question of hemangioma of the duodenum or stomach, perhaps with infiltration of the esophagus. All other possibilities that I mentioned would have to be considered and could not be excluded, nor could their presence be included in any way by the evidence that we have. So far as the lungs are concerned, probably the child had an aspiration pneumonia, the aspirated vomitus and blood first causing atelectasis and then an aspiration pneumonia, with finally a bacterial pneumonia probably superimposed on that.

DR ALLAN M. BUTLER: One thing in the story intrigues me, namely, the nature of the vomitus. The baby was vomiting blood-streaked material and coffee-grounds material with curds. Was there any bile in the vomitus? This might help in determining whether the difficulty was above or below the stomach. The only important feature of the x-ray films is the esophagus, and I should like to ask Dr. Schulz just how impressive the widening is.

DR SCHULZ: The esophagus is somewhat wider than it usually is in youngsters of that age, but I do not know how wide it is in an infant who is vomiting as repeatedly as this child was. There is no gas in the small bowel beyond the duodenum, and none in the colon.

DR BUTLER: The description of the vomitus makes me believe that the lesion was high.

DR NATHAN TALBOT: In postulating an ulcer in the gastrointestinal tract did Dr. Farber assume an associated lesion elsewhere, or would he be surprised to find associated lesions?

DR FARBER: Ulcers in infancy and childhood are usually not associated with changes in other areas.

ushing-Rokitansky ulcers, which are frequently found in the fundus and cardiac end of the stomach, and are either agonal or extremely acute

DR S E THEODORE Was this patient studied for hiatal hernia?

DR FARBER I excluded that in considering the possible diagnosis on the basis of the x-ray findings and surgical exploration. In one or both the evidence should have been found

CLINICAL DIAGNOSIS

Intestinal obstruction due to congenital malformation

DR FARBER'S DIAGNOSES

Duodenal or gastric ulcer?

Hemangioma of duodenum or stomach?

Aspiration pneumonia

ANATOMICAL DIAGNOSES

Esophageal ulcer, traumatic (gavage tube)

Aspiration pneumonia, with multiple pulmonary abscesses

PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMAN The autopsy on this child showed an ulceration measuring about 1.5 cm in length in the lower third of the esophagus about 1 cm above the cardiac orifice. It had eroded the epithelium, and its base was red and granular. We found no other abnormalities in the entire gastrointestinal tract. Microscopically the base of the ulcer was composed of active granulation tissue with well marked capillary proliferation, which suggested that this had been present for quite a while. The right upper and the left middle lobes of the lung contained numerous abscesses filled with polymorphonuclears, and surrounding these were large numbers of monocytes filled with fat. These were beautifully demonstrated in preparations stained with scharlach R. There were also fairly extensive areas of pneumonia around the abscesses.

I believe that we can relate the entire case to the use of the gavage tube before the patient entered this hospital. We inquired and tried to find out how often the gavage tube was used and how long it had been kept down. We could not get the exact information, but apparently it was used many times and was kept down for varying lengths of time. The pulmonary lesions were almost certainly due to aspiration of the vomitus, which must have been mostly milk. It is also possible that at times some of the food fed by the gavage tube slipped down the larynx. This case then is an example of just what can occur as a result of improper use of the gavage tube in premature infants, as stated by Dr Farber in his opening remarks.

DR FARBER I had intended to mention that a few years ago Rector and Connerly² studied the incidence of gastric mucosa in the esophagus, find-

ing it in about 8 per cent of 1000 infants and children. They raised the question of the relation of such mucosa to the formation of ulcers of the esophagus. In this case I do not believe that we have to rely on that explanation.

DR CASTLEMAN This ulcer did not have the fibrinoid base characteristic of a peptic ulcer. It was of good size. I believe that it can be wholly explained on the basis of the gavage tube. Have you not seen ulcers of the esophagus as a result of gavage feeding?

DR FARBER Yes, but never one with a history of bleeding so long as this. This case is truly unique.

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- 1 Hawkins J. Unpublished data
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CASE 31312

PRESENTATION OF CASE

A thirty-two-year-old woman was admitted to the hospital complaining of severe headaches accompanied by nausea and vomiting.

Nine months before admission the patient had become pregnant, and at about the same time she had noted malaise, anorexia and attacks of nausea. She also complained of occasional mild headaches. Ten weeks before admission the headaches became severer and more frequent. Two weeks later, nausea and vomiting appeared and persisted. The patient was hospitalized for a week and showed some improvement following the administration of intravenous fluids and plasma. Four weeks before admission she was again hospitalized, and two weeks later underwent a cesarean section, before the spontaneous onset of labor, because of a contracted pelvis. After this operation the vomiting persisted and became progressively severer. The patient had worn glasses several years for astigmatism. During the month before admission, her vision failed rapidly, so that on admission she could not read but could still distinguish faces. During this period the patient occasionally acted strangely and at times was abnormally moody and sleepy. She had had no convulsions or deafness, but the right side of her body was consistently weak during the two weeks before admission. She had difficulty in naming familiar objects, and there was no other disturbance of speech.

The patient had previously been in good health. About four years before admission she went through a pregnancy without evidence of toxemia, being delivered of a normal, full-term child by cesarean section. Ten years before admission she had complained of vomiting and weight loss for about three months, there was no jaundice, but some abdominal pain.

Physical examination revealed a poorly developed

and nourished woman. The lips and skin were dry. The breasts were enlarged, tender and lactating. The left axillary lymph nodes were tender. The heart and lungs were normal. The abdomen was soft, and no masses were palpable.

The patient was euphonic, and speech was indistinct. Her voice was weak, she lost interest rapidly and had a small range of ideas and a poor memory. The pupils were equal, each measuring 5 mm in diameter, the left was irregular and did not react to light. There were no specific weaknesses of the extraocular muscles, but eye movements were not carried so far to the left as to the right. The patient stated that she had had intermittent diplopia, worse when she was not looking straight ahead. There was papilledema of 3 diopters on the right, and 5 diopters on the left. Visual acuity was greatly diminished. The visual fields were apparently normal. A right facial paresis was present. Auditory acuity was slightly diminished on the left. The neck was slightly stiff, and a Kernig sign was present. Motor weakness was generalized, more marked on the right than on the left. The tendon reflexes were bilaterally hyperactive, particularly on the right, and there was ankle clonus bilaterally, more marked on the right than on the left. The abdominal reflexes were absent. The plantar reflex response was extensor on both sides.

The temperature was 99.2°F, the pulse 100, and the respirations 20. The blood pressure was 110 systolic, 55 diastolic.

The urine on admission contained no sugar but gave a ++ test for acetone, the sediment contained 10 white cells per high-power field. The red-cell count was 3,700,000, and the white-cell count 12,000, the hemoglobin was 11.5 gm per 100 cc.

A lateral x-ray film of the skull showed a calcified plaque in the parietal region. On ventriculography, the fluid in the right ventricle was under increased pressure, which rapidly fell to normal. A large mass appeared to be present in the left frontal region, this markedly depressed the left anterior horn and forced the ventricles, including the third, to the right. The ventricles were not distended. Electroencephalography revealed focal disturbance, greatest in the left frontal region.

A left frontoparietal craniotomy was done on the first hospital day, and 65 cc of thick, brown fluid was aspirated by needle. The patient's immediate postoperative condition was poor. She was unresponsive, with fixed pupils and ankle clonus. All other reflexes were absent. A lumbar puncture revealed slightly bloody spinal fluid under an initial pressure equivalent to 450 mm of water, the final pressure was 100 mm. The blood pressure remained almost constant at 90 systolic, 60 diastolic. The pulse varied from 140 to 160, and the temperature from 100 to 105°F. Although she received 1500 cc of whole blood and 1500 cc of glucose in water, she remained unconscious. A second lumbar puncture

also yielded bloody fluid under an initial pressure equivalent to 400 mm of water, after slow withdrawal of 10 cc the pressure fell to 180 mm.

Late on the first postoperative day the respirations became markedly slowed. An hour later respirations ceased, with persistence of the heart beat for a short time longer.

DIFFERENTIAL DIAGNOSIS

DR JOST MICHELSEN. It is not difficult to decide that this patient had a space-occupying lesion. There were characteristic manifestations of increased intracranial pressure, such as severe headache, nausea and vomiting, failing vision, drowsiness and papilledema. We are also given the localization of the lesion. It involved the left side of the brain, producing weakness of the right side of the body and probably also the disturbances of the oculomotor mechanism by damage to Area 8. The ventriculogram showed a mass in the left frontal region; the electroencephalographic studies were consistent with a lesion there, and I presume that the fluid-containing cavity was found in the same area.

Reviewing briefly some of the signs, I am not certain whether the anomia was actually found on examination or whether some of the patient's complaints were interpreted as an amnesic aphasia. We are not told, either, whether she was right or left handed. If her dominant hemisphere was on the left side, a frontal lesion should have produced a defect in word formation rather than anomia.

Another observation deserves some comment. It is said that the left pupil was irregular and did not react to light and that both pupils were fairly wide and equal. The irregularity may have been due to an old lesion of the iris. The absence of the light reaction probably was the result of severe damage to the left optic nerve, in other words, the patient was blind in the left eye. The fact that the papilledema on the left side was 5 diopters — as compared with 3 diopters on the right side — is certainly suggestive. One would be more certain with regard to this point if the findings on testing the consensual light reaction were known and recorded.

It is obvious that the most important question to be answered in this case is that concerning the character of the mass. If we attempt to make a preoperative diagnosis in the average case we take into account the age of the patient, the history, the situation of the lesion and the radiographic appearance of the skull. In this case we are also informed about some of the findings at operation. The surgeon aspirated 65 cc of thick, brown fluid, which indicates that there was a large cyst, and we shall have to form an opinion concerning the type of the cyst.

The history contains quite a few details of the patient's pregnancy, and this case was announced on the bulletin board as one with cerebral symptoms following pregnancy. Considering all the evidence

ffered, I do not hesitate to disregard the apparent toxemia during the early course of her pregnancy as an etiologic factor. I believe that the appearance of symptoms during her pregnancy — as in some other cases that we have seen — was entirely incidental and perhaps quite misleading to her family physician. Occasionally in a slowly growing tumor exacerbation of manifestations is observed during pregnancy. Dr B Brouwer,* of Amsterdam, observed a patient who, during her sixth pregnancy, developed a bitemporal hemianopsia. It was thought that this was a complication of her pregnancy. Indeed, after delivery her visual fields became normal. With her seventh, eighth and ninth pregnancies she also had transient bitemporal hemianopsia. After delivery of her tenth child, however, the hemianopsia persisted. She then developed headaches, and it turned out that she had a parasellar meningioma.

It is also hardly conceivable that the patient had a parasitic cyst. There was no evidence of cysts elsewhere in the body. There was no eosinophilia. The character of the aspirated fluid was different from that found in a parasitic cyst.

A bacterial infection is quite unlikely, although we are told that the neck was slightly stiff and that a Kernig sign was present. There was no adjacent or distant source of infection so far as we know.

Therefore, we must consider some of the brain tumors in which cyst formation occurs. At this point I should like to ask Dr Schulz to say a few words about the calcification in the occipital region.

DR MILFORD D SCHULZ. The calcification is in the occipital region on the right. It lies fairly close to the midline but scarcely closely enough to the midline to be outside the occipital lobe, it seems to lie above the tentorium.

DR MICHELSEN. Is it quite unlikely that the calcification has anything to do with the mass in the frontal area?

DR SCHULZ. Yes. Certainly there is a considerable distance between the two.

The anteroposterior film shows the deformation and displacement of the frontal horns. The left one is pushed down under the tentorium, and to the right, and the right one and third ventricle are displaced to the right.

DR MICHELSEN. Do you consider that the cyst represents a second lesion?

DR SCHULZ. I think that there were two separate lesions.

DR MICHELSEN. I shall rule out an astrocytoma because of the rapid course of the patient's disease, the absence of epileptic seizures and the character of the fluid. A craniopharyngioma would not have occupied the left frontal lobe, depressing the anterior horn of the lateral ventricle — these tumors arise from below in the suprasellar region. Furthermore, the clinical symptomatology in this case is against such a diagnosis.

*Brouwer B. Personal communication.

A glioblastoma multiforme is a fair possibility. These tumors grow rapidly. The occurrence of hemorrhagic extravasations and necrosis is frequent and would account for the brown color and the consistence of the cystic fluid. We also ought to consider metastatic carcinoma, although there is little evidence in the story to support this diagnosis, except that the patient was in poor shape and had acetone in the urine as an indicator of malnutrition.

There is one other type of tumor, however, in which thick, brown fluid is fairly characteristic. Was a microscopic examination done on the fluid?

DR CHARLES S KUBIK. That was done, and there were large vacuolated cells that probably contained fat. Such cells are present in the cystic fluid of various kinds of tumors. There were no cholesterol crystals.

DR MICHELSEN. Dr Kubik has anticipated my thought. I had in mind a dermoid cyst. These tumors are rare. They are usually located in the midline, basally, but they may occur in the different lobes of the forebrain. At times they are multiple. They grow at a very slow rate and may attain a considerable size before resulting in symptoms.

Now let us search for the cause of death. This patient was a nearly hopeless surgical problem from the onset. Her general condition and nutrition were poor, as mentioned before. She had bilateral pyramidal-tract disturbances, which I have omitted from the discussion so far. They, and possibly also the rigidity of the neck and the Kernig sign, seem to indicate that there was some tentorial herniation preoperatively as a result of markedly increased intracranial pressure. This condition apparently was not relieved by the removal of the cyst fluid, indeed it progressed, and the two postoperative lumbar punctures certainly did not help the situation. The patient developed hyperthermia and respiratory failure.

In conclusion, I should say that this patient had a brain tumor and that during the last few days of life a tentorial pressure cone occurred, which resulted in death. The tumor may have been a malignant, necrotic, hemorrhagic glioma, a dermoid cyst or possibly a metastatic carcinoma. I am prepared to hear that it was none of the three.

DR BENJAMIN CASTLEMAN. Would you like to say a word about this patient's pregnancy, Dr Newell?

DR JOHN L NEWELL. I do not see how the tumor could have been associated in any way with the pregnancy, which was a full-term cesarean delivery. The vomiting and headache were probably passed off as being due to the pregnancy, and this was undoubtedly misleading.

CLINICAL DIAGNOSES

Brain tumor
Respiratory failure

DR MICHELSEN'S DIAGNOSES

Brain tumor (glioma, dermoid cyst or metastatic carcinoma)
Tentorial pressure cone

ANATOMICAL DIAGNOSES

Adenocarcinoma of lung, with metastases to bronchial lymph nodes and brain.
Tentorial pressure cone, with cerebral infarction.

PATHOLOGICAL DISCUSSION

DR CASTLEMAN Before I tell you what was found at autopsy perhaps Dr Kubik would like to tell what was found in the brain grossly

DR KUBIK In the left frontal region there was a tumor a large part of which was taken up by a cystic cavity measuring 2.5 cm in diameter and containing a small amount of coagulated brownish fluid. The cavity was naturally much larger before the cyst was drained at operation. There was an exceedingly large temporal pressure cone on the left side, and a smaller one on the right, with resulting compression of the midbrain. The aqueduct was flattened to the point of obstruction. There was a small hemorrhage in the midbrain in the region of the third-nerve nuclei. Either the compression of the midbrain or the implication of the third nerves might have accounted for the diplopia and the dilated fixed pupils. There was also extensive, recent, hemorrhagic necrosis of a large part of the left cerebral hemisphere. Such necrosis, resembling hemorrhagic infarction, is not infrequently ob-

served with a temporal pressure cone, but the infarcted region is usually the one supplied by the posterior cerebral artery, presumably because this artery is compressed by the inner edge of the tentorium. I do not know how to account for infarction in this case, because the infarcted regions are supplied by both the posterior and middle cerebral arteries. There was also a large cerebral pressure cone, which no doubt accounted for the respiratory paralysis. It is reasonable to suppose that both the temporal and the cerebellar pressure cones were made worse by the lumbar punctures.

DR CASTLEMAN The tumor microscopically was a metastatic carcinoma. The primary source was in the right upper lobe bronchus. Unfortunately an x-ray film of the chest was not taken. There was an ulcerating tumor in the bronchus, with extension to the surrounding parenchyma of the lung and with metastases to the bronchial lymph nodes.

The uterus was enlarged. It had not completely involuted, and in the endometrium were shaggy clots, which allowed us to toy with the idea, based on the gross findings, that it was a chorionepithelioma with metastases to the lung and brain. Histologically, however, the tumor was an extremely rapidly growing adenocarcinoma and not a chorionepithelioma.

The pregnancy may well have made the tumor grow much faster, and this rapid growth of the tumor cells may have accounted for the fact that the tumor was cystic, that is, it had broken down because it had outgrown its blood supply. The bronchial lymph nodes were also necrotic.

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PHYSICAL FITNESS AFTER THE WAR

THE ineligibility for military service of over 30 per cent of the men examined under Selective Service is one of the outstanding health facts uncovered by the war, and those who have used the war as a sounding board for their prewar convictions are already exploiting this fact by resolving in public, as usual, that such a thing must never happen again. To say, on the other hand, that physical standards for large bodies of men were never before so high as they are in our armed forces is merely to state the obvious. So far as the medical profession is concerned, it has a definite obligation to give this matter its attention, to formulate its opinion and to raise its voice in the current political discussion.

How can we reduce to a minimum the physical defects of another generation? There are, to begin with, certain obstacles of an emotional nature with which we shall continue to contend, and we must also recognize the biologic fact that no seed is of uniformly high quality. Nurserymen and raisers of livestock know that nature with its infinite variety, produces, even with the best seed and stock, a considerable percentage of imperfectly formed specimens — stunted plants or runts. The nurseryman and farmer cull these from their crop or herd, being under no compulsion to raise them, although of course, they could, with time and patience, nurse many of them to maturity. We have no such freedom of action in human nurseries. Ours is a civilization in which we strive for the protection and survival of the unfit.

The medical profession's major activities have for years been concerned with such protection and survival, and in view of its accomplishments and its support by the public it is today actually responsible for the survival of many of those who have been found ineligible for military service, in other words, we have reversed the philosophy and the practice of the ancient Spartans. We must also recognize that, in many places, legal and political impediments have been placed in the way of parents who may have biologic as well as economic reasons for controlling the birth of their offspring. These are the obstacles — paradoxical and perhaps insurmountable — with which our civilization contends and will contend at the close of the war. In view of them the conditions revealed by the statistics of the Selective Service and induction boards are not at all amazing, they are only what might have been expected, although many of us have been startled by the fact in this period of national crisis.

The greatest difficulty with which we are confronted in attempting to reduce the numbers of the physically unfit in a democracy is the freedom of the individual to neglect himself. It would be a good freedom to abolish if such a thing were justifiable, and the medical profession should support any reasonable steps likely to promote physical fitness.

At the present time there are two political rings into which the profession can throw its hat. The first is the constructive health-education program

that has been adopted by many cities and towns outside Boston, largely owing to the efforts of the Massachusetts Department of Public Health and Department of Education, and that is recommended by the Strayer Report as a procedure that might well be adopted in the schools of Boston. This is something that doctors can approach locally, where they can tactfully secure what intimate knowledge of existing conditions is necessary to initiate a reform, good medical leadership of this type being seldom challenged. The other political ring is that which encircles those who are now debating peacetime military training. Here will be found a sharp cleavage of opinion — one in which the clergyman, the professional soldier, the statesman, the businessman, the educator and many other intelligent people are divided among themselves. This being so, and in view of the biologic and psychologic facts that every doctor knows, it is the duty of organized medicine and of each individual physician to throw themselves vigorously into the debate in favor of peacetime conscription.

Even in wartime the Army has rehabilitated close to two million men, in peacetime it could unequivocally eliminate many of the correctible defects that are now neglected by parents, school authorities and individuals. Universal military training in peacetime would do more to improve the physical fitness of the Nation's young men than any other method that could be devised. There should be no division of opinion in the medical profession on this issue.

SPREAD OF STREPTOCOCCAL INFECTIONS

DURING World War I, hemolytic streptococcus infections were the most serious and the most frequent complications of measles and influenza, as well as of wounds, and they probably accounted for a great many of the deaths ascribed to these conditions in the United States Army. The rapid spread of such infections in Army hospital wards was the subject of numerous studies at that time. The recognition of specific groups and types of hemolytic streptococci during the last decade has given epidemiologists a highly useful tool whereby they can trace the sources and spread of such infections with

reasonable assurance and accuracy. Although hemolytic streptococcus infections are not nearly so prevalent now, either in civilian or in military populations, as they were during the first world war, they still constitute an important problem at certain Army and Navy installations. Hence, various groups of workers have been engaged in studying these infections. Among them, the Commission on Air-Borne Infections has obtained useful information concerning the quantitative aspects of the transmission of hemolytic streptococci in Army hospital wards.

Hamburger,¹ in a report of some of these studies, re-emphasized certain of the known facts and brought out some new and useful ones that are essential for the control of infections with these organisms. He found, for example, that gross infections by hemolytic streptococci on open wards may spread rapidly when only as few as one or two carriers are originally present. On the other hand, as many as 50 per cent of the patients on a ward may harbor Group A streptococci in their throats without cross infection's occurring in any of the others. On the average, the carrier rate for a specific type known during the same season to be invasive may be as high as 19 per cent without the occurrence of cross infection. "Subclinical cross infection," that is, a spread of carriers or of cases of mild infection by hemolytic streptococci, was quite frequent.

As already indicated, outbreaks of measles have been known to encourage the spread of hemolytic streptococci and to give rise to serious respiratory complications with these organisms. During the present war, cases of German measles have been unusually prevalent. This disease is ordinarily considered to be a mild one of little or no consequence. In the present investigations, however, Hamburger found that patients recovering from German measles share the well recognized susceptibility of those with measles to streptococcal infections.

In the course of tracing the origin of cross infections with streptococci, emphasis was placed on the importance of typing the streptococci before a member of the hospital personnel who is a carrier can be incriminated as the source of the infection. Actual typing under such conditions may indicate that an entirely different strain is responsible for

the cross infection than the one or ones found in the carriers among the personnel. This may also be of importance in surgical practice, where the spread of streptococcal wound infections is often ascribed to a surgeon or an operating room nurse who happens to be a carrier. Such persons are often kept from the operating rooms when they are not the ones responsible for the cross infections.

Attempts were also made to determine to what extent streptococcus carriers may disseminate their strains.² This was done by comparing the results of throat cultures with quantitative estimations of the numbers of organisms in the saliva, the latter being presumed to be the origin of droplets from which the organisms get into the air and dust. It was found that a person with a positive throat culture may or may not have the same organism in the saliva. In cases of active sore throat, to be sure, over 80 per cent of the specimens of saliva contained the same strains of streptococci as were found in the throat cultures but the rest had no streptococci in the saliva. The relation of the positive throat and salivary cultures in any patient varied from day to day. In about half the cases the number of hemolytic streptococci in the saliva diminished in successive samples, usually gradually but sometimes quite abruptly. In about a fourth of the cases the results of repeated cultures were the same over a period of weeks, about half of these having positive and the other half negative cultures of the saliva. Cases of scarlet fever and those of pharyngitis or tonsillitis without a rash behaved alike with respect to the number of streptococci in the saliva. Tonsillectomized patients tended to carry fewer streptococci in the saliva, and for shorter periods, as compared with those who had tonsils. None of these findings had any relation to the type of the streptococci. Interestingly enough, treatment with sulfonamides did not permanently eliminate or decrease the numbers of hemolytic streptococci either in the throat or in the saliva.

Since the commission was interested primarily in air-borne infections they made extensive studies of hemolytic streptococci in the air, floor dust and bedclothes in the hospital wards.³ The great difficulty of proving that cross infections in a ward are truly air borne, and not spread by contact, was emphasized.

One case was noted of a technician in whom there was a strong suspicion of accidental air-borne infection from prolonged exposure at a distance from patients. This technician was engaged in taking air samples and it was calculated that the total dose that she inspired was about 13,000 organisms.

Many known epidemiologic facts about hemolytic streptococcus infection in the environment were confirmed by accurate methods. It was found, for example that the rise and fall in the number of streptococci in scarlet-fever and sore-throat wards paralleled the fluctuations in the total numbers of bacteria in the air although the streptococci constituted a small part of the total. Most of the other organisms were saprophytes and, therefore probably arose from dust and bedclothes, which contain tremendous numbers of bacteria. Pockets of high concentrations of hemolytic streptococci were associated with high concentrations of saprophytes during periods of sweeping or bedmaking. The largest numbers of streptococci were found in the air dust and in the bedclothes nearest those patients who actually eliminated the largest number of streptococci.

On the basis of their observations, the members of the commission were not able to determine accurately the exact role of air-borne and dust-borne infections. They suggested however, that the control of air-borne streptococci in hospital wards may be largely a question of controlling the secondary reservoirs of these organisms in the dust and bedlinens. The results of studies in which this was attempted seem to indicate that such control is feasible. The maximum reductions in air-borne streptococci were observed when oiling of the bedclothes and floors was used in conjunction with glycol vapor.⁴

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MASSACHUSETTS MEDICAL SOCIETY

DEATH

TALTY — Francis E. Talty, M.D., of Hoboken, New Jersey, died on May 27. He was in his sixty-sixth year.

Dr. Talty received his degree from Harvard Medical School in 1906. He was a member of the New England Roentgen Ray Society.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JUNE, 1945

RÉSUMÉ

DISEASES	JUNE 1945	JUNE 1944	SEVEN YEAR MEDIAN
Anterior poliomyelitis	2	1	1
Chancroid	1	4	*
Chicken pox	1282	1748	1170
Diphtheria	14	6	7
Dog bite	1299	1186	1414
Dysentery bacillary	1	2	2
German measles	139	199	199
Gonorrhea	378	442	355
Granuloma inguinale	0	0	*
Lymphogranuloma venereum	1	4	1
Malaria	92	59	3918
Measles	1409	3011	16
Meningitis, meningococcal	19	28	44
Meningitis, Pfeiffer bacillus	2	0	31
Meningitis, pneumococcal	3	3	0
Meningitis, staphylococcal	0	0	21
Meningitis, streptococcal	2	0	0
Meningitis, other forms	2	1	2
Meningitis, undetermined	3	7	47
Mumps	1677	966	877
Pneumonia, lobar	140	215	225
Salmonella infections	18	13	6
Scarlet fever	949	899	791
Syphilis	335	458	417
Tuberculosis, pulmonary	213	287	287
Tuberculosis, other forms	15	21	24
Typhoid fever	2	2	7
Undulant fever	6	5	4
Whooping cough	560	248	551

*Made reportable December, 1943

†Four-year average

COMMENT

Only two cases of anterior poliomyelitis were recorded in June. It should be pointed out, however, that no conclusions can be drawn from this fact with reference to the likelihood of an outbreak later in the season. Even the July figures are not always an accurate indication of what to expect.

Lobar pneumonia showed a very low incidence — the lowest for June since 1922.

Mumps was at the lowest point of this year but was, nevertheless, at the highest level of any June on record.

Diphtheria was still higher than in recent years. Only once since 1937 has June shown as many as 14 cases.

Only once before have more than 18 cases of Salmonella infections been reported in June.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Haverhill, 1, Holyoke, 1, total, 2.

Diphtheria was reported from Boston, 3, New Bedford, 2, Newton, 1, Norwood, 1, Somerville, 5, Taunton, 1, Worcester, 1, total, 14.

Dysentery, amebic, was reported from Regional Hospital, Waltham, 1, Camp Edwards, 2, total, 3.

Dysentery, bacillary, was reported from Wrentham, 1, total, 1.

Malaria was reported from Arlington, 1, Boston, 3, Camp Edwards, 17, Fort Devens, 55, Gloucester, 1, Lawrence, 1, Norwood, 1, Somerville, 1, Springfield, 1, Waltham Regional Hospital, 11, total, 92.

Meningitis, meningococcal, was reported from Attleboro, 1, Boston, 6, Dedham, 1, Fall River, 1, Holyoke, 2, Ipswich, 1, Lynn, 1, Malden, 1, Newton, 1, Norwood, 1, Quincy, 1, Randolph, 1, Topsfield, 1, total, 19.

Meningitis, Pfeiffer-bacillus, was reported from Arlington, 1, Cambridge, 1, total, 2.

Meningitis, pneumococcal, was reported from Boston, 1, total, 3.

Meningitis, streptococcal, was reported from Boston, 1, Worcester, 1, total, 2.

Meningitis, other forms, was reported from Boston, 2, total, 2.

Meningitis, undetermined, was reported from Brookline, 1, Springfield, 2, total, 3.

Salmonella infections were reported from Boston, 3, Cambridge, 1, Haverhill, 1, Malden, 1, Marblehead, 6, Newton, 2, Northampton, 1, Salem, 2, Wellesley, 1, total, 18.

Septic sore throat was reported from Boston, 4, Easton, 1, Haverhill, 1, Lynn, 6, Medford, 1, Sharon, 1, Williamstown, 3, total, 20.

Typhoid fever was reported from Lowell, 1, New Bedford, 1, total, 2.

Undulant fever was reported from Adams, 1, Dighton, 1, Sheffield, 1, Waltham, 1, West Boylston, 1, Williamstown, 1, total, 6.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Lowell	August 3	Albert H. Brewster
Springfield	August 21	Garry deN. Hough, Jr.
Fall River	August 27	Eugene A. McCarthy

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Textbook on Pathology of Labor, the Puerperium and the Newborn. By Charles O. McCormick, M.D., clinical professor of obstetrics, Indiana University School of Medicine, and consulting obstetrician, William H. Coleman Hospital for Women, Indianapolis City Hospital and Sunny Side Sanatorium. 8th, cloth, 399 pp., with 191 illustrations, including 10 in color. St. Louis: The C. V. Mosby Company, 1944. \$7.50.

The author's lectures, prepared for the senior medical students at Indiana University, have served as a basis for this new work on the pathology of labor. An attempt has been made to set forth only the essentials of present-day obstetrics, purposely avoiding confusing textbook material. Special consideration has been given pelvimetry, breech extraction, placenta previa, post-partum hemorrhage, use of forceps, version and cesarean-section techniques, puerperal infection, breast pathology and asphyxia neonatorum. There are detailed descriptions of therapeutic and surgical procedures, of tubal sterilization operations and of the newer therapeutic adjuncts, such as puerperal sterilization, sulfonylamides, penicillin and stilbestrol, vitamin K, erythromycin and improved analgesia. The book is well illustrated and printed on good paper. References to medical literature have been incorporated in the text instead of placing them at the end of chapters.

Technique of the Standard Kahn Test and of Special Kahn Procedures. By Reuben L. Kahn, chief of clinical laboratories, University of Michigan Hospital. Revised and enlarged edition. 8th, paper, 52 pp., with 4 tables. Ann Arbor: University of Michigan, 1944. 25 cents.

In this revised and enlarged outline, Dr. Kahn presents the technique of the standard Kahn test with serum and spinal fluids, the interpretation of precipitation results and techniques of special procedures, with an appendix on the preparation and standardization of antigen. The pamphlet is divided into four parts, with an appendix apparatus, reagents, standard Kahn procedures, and special Kahn procedures.

(Notices on page xvii)

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SENILE PSYCHOSIS AND PELLAGRA*

A Report of Two Cases

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CHARLOTTESVILLE, VIRGINIA

SEVERAL patients with psychoses of the senile type have been observed to improve after a period of therapy with niacin, thiamine, riboflavin and substances rich in the vitamin B complex. Review of their records has shown 2 with atypical pellagra. In view of the probable relation of pellagra to the clinically observed psychoses, these cases will be reported. The number of cases observed is not sufficient to warrant a statistical analysis, but the indications are that they are not infrequent

* * *

The neuropsychiatric manifestations of pellagra in the early stages of the disorder are vague, consisting of irritability, weakness, lassitude, skeletal pains and severe malaise. As the disease advances more definite syndromes may appear—depressive states, manias, paranoid states, acute confusional states, agitated anxiety states and hallucinatory states. In the end stages, evidence of severe neurologic impairment may develop—stupor, convulsions, incontinence, impaired thermal regulation, muscular rigidity, irregular involuntary movements of the musculature, hypertonia, defective sensation and muscle paralysis. The manifestations may be solitary or occur in various combinations.¹⁻⁹

Neurohistologic studies performed on pellagrins have revealed atypical neuronal and capillary changes distributed throughout the neuraxis,¹⁰⁻¹³ especially in the cerebrum. Within the cortex the ganglion cells may lose their Nissl substance and eventually disappear. The extent of this change varies from case to case, as a rule it is most noticeable in the frontal lobes and in the hippocampus. In addition, there may be proliferation of glial tissue and of the endothelium of small vessels. In the subependymal regions the proliferative reaction may be the most noticeable.^{10, 11} Circumscribed parenchymal changes are usually associated with such vascular lesions. These reactions are to be found in a wide variety of so-called "toxic"

encephalopathies (central neuritis), as well as in pellagra.

Pellagrins with neuropsychiatric disorders have been treated successfully with niacin.¹⁻⁶ Some investigators have presented evidence that the results are more satisfactory when niacin is supplemented with other vitamins of the vitamin B group and a well balanced diet.^{2, 5, 14}

The neuropsychiatric disorders that accompany old age may be considered in two categories—those arising primarily in the brain tissue and those secondary to an impaired circulation.

The first is an involution, a natural consequence of aging. It varies in intensity from a mild forgetfulness and a tendency to reminisce to extreme confusion, disorientation and dementia. The usual occurrence is in the years beyond the eighth decade, but similar conditions are known to affect persons in earlier life. When severe, the latter group may give rise to presenile dementias. These conditions are insidious and progress slowly.^{15, 16} The pathologic alterations in the brains of patients so affected are notably a loss of neurons, neurofibrillary degeneration and the development of senile plaques or collections of amorphous deposit. Such changes are most noticeable in the frontal-lobe cortex, the Purkinje-cell layer of the cerebellum and the striatal portion of the basal ganglia.¹⁷ Often there is a wide discrepancy between the severity of the clinical disorder and the extent of the pathologic change within the brain.^{17, 18}

In the second type, the clinical disturbances are due to loss or impairment of parenchymal function as the result of impaired circulation. The syndromes produced may simulate those seen in the more advanced cases of the previous group, but oftener signs of focal lesions are present—hemiplegia, aphasia, agnosia and similar manifestations. The patients with vascular affection are more strikingly confused and disoriented than those in the other category, they have more vivid hallucinations. Lesions are likeliest to occur in the regions supplied by the middle cerebral artery and its branches. The size and extent of lesions vary from small

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†Formerly resident neuropsychiatrist, University of Virginia Hospital.

ischemic foci involving the cortex alone to large infarctions affecting the whole hemisphere

Although the differences between these two groups of patients may be recognized in some cases, Critchley¹⁷ has stated, "We must admit that the distinction is more academic than practical, since in the great majority of cases the process of aging operates simultaneously on both the parenchyma and the blood vessels of the brain"

The occurrence of so-called "senile psychosis" in association with pellagra was noticed by Singer,⁸ who concluded that in these cases pellagra is only incidental. Lorenz⁹ observed a similar coincidence. He wrote

Chronic mental states largely ascribed to pellagra are those occurring late in life. A number of cases were observed showing typical senile dementia. These were all advanced in years and the occurrence of mental defects of this nature would have been expected. Likewise, a number of cases with marked peripheral arteriosclerosis showed a general mental enfeeblement such as is usually associated with sclerosis of the cerebral vessels. That these may have developed at a somewhat earlier period owing to the pellagra is not questioned. These are probably instances in which pellagra served as a precipitating factor in the development of a psychosis of the senile or vascular type

Rainsford,¹⁹ Bonhoeffer,²⁰ Bigland²¹ and McGregor²² have reported cases that could have been similarly classified. Chittick and Stotz²³ quote Tompkins as stating that of 25 patients recovering from senile psychoses, 5 had had glossitis during the early stages of hospitalization, and this finding is believed by them to have been indicative of a nutritional deficiency state. Rothschild and Sharp²⁴ and Woltman²⁵ stress the importance of adequate nutrition in maintaining cerebral function in aged persons. Robinson²⁶ describes "toxic-delirious reactions of old age" and mentions the importance of metabolic and nutritional disturbances in precipitating such reactions. Wadsworth et al²⁷ used vitamin B complex in the treatment of an unselected group of senile psychotic patients, with indifferent results. Palmer and his co-workers²⁸ reported on a group of 123 institutionalized senile psychotic patients, 30 of these recovered when given supportive therapy, which included large doses of vitamin preparations.

In neurohistologic studies of pellagra, Singer and Pollock¹² noted the occurrence of neurofibrillary ganglion-cell degeneration in some specimens, but made no mention of the ages of the patients from whom these were taken. Pearson¹³ encountered a case with a clinical picture of a senile psychosis among a group of patients in whom central neuritis was found at autopsy. Although none of these findings are conclusive, they indicate the possibility of a closer relation between some of the senile psychotic episodes and pellagra.

CASE REPORTS

CASE 1. E. D., an emaciated 55-year-old woman, was admitted to the neuropsychiatric service of the University of Virginia Hospital on September 6, 1942. Her illness had

begun late in 1929 with severe pains in the lower extremities. This was followed by progressively increasing weakness, which necessitated her remaining in bed. In addition, mental symptoms appeared, notably irritability, contrariness and emotional instability. Within several months after the onset the patient's appetite had failed and her food intake had decreased to half the usual quantity.

In the 9 succeeding years there were brief periods of partial remission, but otherwise the clinical picture remained unchanged despite medical care. In the summer of 1939 the patient became semistuporous and remained in that state for nearly a month. As a sequel to this, her intellectual function deteriorated further and her weakness increased. No further remissions occurred.

During the early part of 1942 the patient's emotional symptoms became exaggerated. On August 21, 1942, she lapsed into a stupor that persisted for 4 days. Recovery after this was very poor and the patient was hospitalized.

On admission the patient was confused, disoriented and agitated and complained of pains throughout the body. She was easily distracted, expressed paranoid and depressive ideas and prattled extensively. She had auditory and visual hallucinations of a morbidly violent character, which caused restless overactivity and often interfered with sleep. She echoed the gestures and speech of the examiner but was unable to perform skilled movements. She was moderately aphasic.

Physical examination revealed a dry skin. There were seborrheic excrescences in the nasolabial folds and macerations at the corners of the mouth. The oral and pharyngeal mucous membranes were dry and reddened. The tongue was magenta red. There were two shallow ulcers approximately 0.5 cm in diameter on the posterior wall of the pharynx. The cardiovascular and respiratory systems were not unusual. The abdomen was normal. The musculature of the extremities was wasted and tender on deep pressure. The patient was unable to arise from bed because of generalized weakness. All the tendon reflexes were hyperactive, except at the left patella. Abdominal reflexes could not be elicited. The plantar reflexes were normal. Vibratory and position senses were severely impaired, producing a stereoaesthesia. Other neurologic findings were normal.

The red-cell count was 4,030,000, and the white-cell count 6600, the hemoglobin concentration was 12 gm per 100 cc. The blood sugar concentration was 46 mg per 100 cc, and the urea concentration 46 mg. Wassermann and Kahn reactions were negative. The urine was normal. Gastric analysis showed 12 units of free acid.

At the time of admission the patient refused to eat and had to be fed by gavage. Two days following admission treatment was instituted with large doses of nicotinic acid amide, riboflavin, brewers' yeast powder and thiamine chloride. By the 6th day she was able to eat. The oral and nasolabial lesions cleared by the 7th day. The patient's mental acuity increased gradually and the bizarre patterns of thought disappeared, but the emotional lability persisted. In the early part of October treatment was supplemented with intramuscular doses of crude liver extract. During the month intellectual function improved surprisingly, but the tongue remained magenta red, and the emotional reactions immature.

The patient was discharged on October 25. During the succeeding 2 months she remained well, but shortly after Christmas she again became irritable and lost her appetite. In late January, 1943, soreness of the tongue developed and the patient sought readmission.

At the second admission, the patient complained severely of gastrointestinal discomfort. Clinical, roentgen-ray and laboratory examinations revealed no organic lesion in the stomach or bowel. After treatment with crude liver extract and brewers' yeast powder there was gradual improvement, but vague neurotic complaints persisted. At no time did the magenta-red color of the tongue disappear. Treatment was continued after discharge, and no further recurrences were noted over a 10-month period.

*The daily dosages of vitamins were as follows: nicotinic acid amide, 0.6 to 1.05 gm in divided doses by mouth; riboflavin, 0.01 to 0.02 gm by mouth; thiamine chloride, 0.050 gm parenterally and brewers' yeast powder, 15.0 gm by mouth.

†The daily dose of crude liver extract (Lederle No. 9083-291811) kindly supplied through the courtesy of Lederle Laboratories Incorporated, Pearl River, New York, was 5 cc.

‡A full scale Wechsler-Bellevue test on October 22 revealed an IQ of 125.

Comment The duration of the disease in this case was unusual since one would not expect improvement of such degree after this length of time. The late manifestations were like those of a vascular disturbance, although the earlier ones were neurasthenic. The latter disturbances, the memory defects and the confabulatory episodes resembled the Korsakoff syndrome, which may occur in either the senile psychoses or in pellagra. The episodes of stupor were similar to those described in pellagrins by Cleckley and his co-workers.³ The skin lesions were those of riboflavin deficiency, and the mucosal alterations were the combined effect of several deficiencies. The response to treatment puts this case definitely in the pellagra group.

CASE 2 R. L. B., a 78-year-old man, was admitted to the medical service of the University of Virginia Hospital on October 31, 1942. Three days preceding admission he suffered a "stroke" and as a result became irrational.

Six years prior to admission he was hospitalized for an acute otitic infection. At that time he had choreiform tremors, but these were not described further. The blood pressure was then 150/85 and the urine had a specific gravity of 1.022 and was otherwise not remarkable. At a subsequent examination in 1938, no mention was made of any tremor. From 1939 to 1942 the patient had been under the care of his family physician for hypertension. During the last-mentioned year he had been having frequent slight "strokes" that resulted in progressive impairment of locomotion and in transient confusional states. The lower extremities "felt like blocks of wood" and he could not be sure of their position. On October 24, 1942, he suddenly became confused and lost the power of speech. He refused all food and fluid, developed a fever and within a few days became completely irrational.

At the time of admission the patient was noisy, inattentive and easily distracted. His emotional reactions were labile and he was overly concerned with religious matters. Motor and sensory aphasia, echolalia, echopraxia and perseveration of responses were present. The bladder and bowels were incontinent.

On physical examination, cachexia was noticeable. The skin was dry and thickened. The conjunctivas and scleras were hyperemic. The retinal vessels were slightly narrowed. The mucous membranes of the mouth and pharynx were reddened and edematous. A few carious teeth remained in the lower jaw, the periodontal tissues were severely infected. The skin of the chest was covered with the lesions of a seborrheic dermatitis. The lungs were normal. The heart was clinically enlarged, and the rhythm was irregular owing to numerous extrasystoles. The blood pressure was 220/120. There were reducible bilateral inguinal hernias. A shallow decubitus ulcer overlay the sacrum. There was extensive peripheral arteriosclerosis. There were uncontrolled irregular movements of the extremities. The musculature was weak and wasted. All the tendon reflexes were hyperactive, especially on the right side. The abdominal reflexes were easily fatigued. The right plantar reflex was extensor and the left one normal. The special senses could not be evaluated, but otherwise the functions of the cranial nerves appeared normal. General sensibility was such that only strong thermal and painful stimuli evoked any responses. Sucking reflexes could be elicited, and a grasping response was present in the right hand.

The red-cell count was 5,300,000 and the white-cell count 12,000. There was a hemoglobin concentration of 16.5 gm per 100 cc, and a blood urea concentration of 86 mg. The Wassermann reaction was negative. The plasma carbon dioxide combining power was 58.6 vol per cent. The urine contained a small amount of albumin and an occasional leukocyte was seen in each high-power field of the sediment. The cerebrospinal fluid was normal.

Several hours after admission, treatment was started with infusions of physiologic saline solution containing 5 per cent of glucose. On the following morning the red-cell count was 4,700,000, the hemoglobin concentration 13 gm per 100 cc and the urea concentration 53 mg. The urine did not contain measurable amounts of albumin. Infusions were administered over the next few days, without change in the neuropsychiatric picture, and the patient was transferred to the closed ward.

On the 5th day, the treatment was modified to include large doses of nicotinic acid amide, thiamine chloride, ribo-

flavin and brewers' yeast powder.* Within 3 days the disturbances of speech and behavior cleared and the patient became tidy and co-operative. By the 15th day all neurologic signs had returned to normal and the parenteral vitamin and saline therapy was discontinued. The patient's condition continued to improve steadily, his memory returned except for the period of his confusion, and he stated that he felt as though he had had a bad dream. He was discharged on the 23rd day, and remained well for the succeeding 9 months.

In the latter part of August, 1943, the patient became quite stubborn. Periodically thereafter he was confused, ordered his wife and daughter from the house, and on one such occasion attempted to beat them. By October he refused all nourishment except an occasional teaspoonful of milk.

On October 10 the patient suffered a series of convulsive seizures, and on October 12 he was readmitted to the neuropsychiatric ward. Examination at that time revealed severe dehydration. There were pellagrous skin changes on the hands and other exposed parts. The mucous membranes of the mouth and pharynx were reddened, and there was a small ulcer in the pharynx. The conjunctivas were injected. The cardiac status was not different from that of the previous admission. The blood pressure was 215/115. The patient was dysarthric, disoriented as to time and place, restless, inattentive and confused. No significant changes were noted in the eye grounds. The tendon reflexes were normal. The abdominal reflexes could not be elicited, and the plantar responses were flexor Hoffmann's sign was positive in the left hand. Sensory examination demonstrated much the same phenomena as those elicited on the preceding admission. Co-ordination was so poor that the patient was unable to stand even with assistance. Laboratory studies revealed no significant deviations from the normal.

On the day following admission administration of large doses of the crystalline vitamins was started. Within a week all the oral and skin lesions had healed. The patient's emotional reactions improved and he regained the use of his extremities in locomotion. During the hospital stay the blood pressure fluctuated widely but usually remained below 150/90. The patient was discharged 11 days following admission, at which time there were no clinical signs of the neuropsychiatric disturbance. Re-examination over a 4-month period indicated continued minor emotional instability, although the patient was receiving maintenance doses of nicotinic acid amide.

Comment This case illustrates the effect of nutritional inadequacy in a patient with a subclinical encephalopathy of the combined senile-vascular type. The re-establishment of adequate neurologic function and the concurrent disappearance of the somatic signs of deficiency under quasi-controlled therapy indicate that the neuropsychiatric dysfunction was related to the biochemical imbalance. The status of the patient between exacerbations suggests that the clinical picture in the acute phases was largely determined by the underlying aging processes within the brain.

DISCUSSION

The neuropsychiatric manifestations of pellagra usually appear after dermal, oral or gastrointestinal manifestations have developed. In a small proportion of cases, however, neuropsychiatric signs alone are manifest. Elvehjem¹⁴ in reviewing the relation between nicotinic acid and pellagra observed that central nervous tissue retained its ability to oxidize glucose even with severe diminution of the concentration of co-enzyme in the tissue fluids. Such a finding indicates that other factors may play an important role in altering the so-called "resistance of nervous tissue to nicotinic acid deficiency."

*The daily dosages of vitamins were as follows: nicotinic acid amide 0.1 gm intravenously; riboflavin 0.01 gm; thiamine chloride 0.05 gm intravenously; and brewers' yeast powder 15.0 gm.

The major neurohistologic changes in the senile psychoses and in pellagra overlap somewhat in the frontal lobes and in the deeper ganglions. A combination of these two pathologic processes may result in clinical disturbances when either alone is of insufficient magnitude to produce symptoms. Under these conditions a clinical neuropsychiatric disorder may be present with but minimal extraneural signs of pellagra.

The senile person is apt to become mentally disturbed during the course of acute febrile illness, following severe trauma and under emotionally unfavorable conditions. As yet, this liability has not been fully explained. This type of occurrence is evidence of the increased susceptibility of the aging nervous system to adverse environmental changes. Such susceptibility may be attributable to the organic changes within the nervous systems of such patients, just as are the personality changes of the aged.

Personality changes also become manifest in the dietary. Restrictions, both qualitative and quantitative, are not infrequent among elderly patients. Fadism of this sort tends to eliminate valuable foodstuffs from the diet, and its continuation may lead to clinical deficiency states. In this way a cycle is formed in which a fad leads to an inadequate food intake, and the inadequacy to a further loss of appetite and a severer dietary restriction.

The diagnosis of pellagrous encephalopathy in the aged person with psychosis must depend on clinical or laboratory evidence of nicotinic acid deficiency. The neuropsychiatric syndromes produced are not characteristic of pellagra but of the location of the lesions in the central nervous system, and they may occur in a variety of disorders. The response to controlled therapy may be of value in this regard, in which case the diagnosis may be made in retrospect. In general, mucosal and dermal lesions of nicotinic acid or riboflavin deficiency should be sought whenever an aged psychotic patient is examined. Evidence of other nutritional disorders should lead one to investigate further.

Treatment should be largely prophylactic. Persons in the late decades of life should have diets of optimal rather than minimal adequacy. When the maintenance of an adequate diet becomes infeasible, dietary supplements should be administered. For this purpose, either the crystalline vitamins or concentrated extracts may be used. Crystalline preparations may be given parenterally to patients whose intestinal absorption is defective. When deficiency already exists, effective treatment should combine

the above modes of administration. Adequate returns may be expected from adequate nutrition, even in the aged.

SUMMARY

Senile psychosis may be simulated by pellagrous encephalopathy in the aged. The underlying neurologic alterations in the elderly patient may predispose to this occurrence.

The senile-pellagrous type of encephalopathy may respond well to treatment with crystalline vitamin B products or with natural vitamin B concentrates. The recognition of this group of cases may permit effective therapy.

The maintenance of an optimal dietary by the normal aged person as well as by the senile invalid should be a matter of primary importance.

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ACUTE INFECTIOUS LYMPHOCYTOSIS IN YOUNG ADULTS

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ACUTE infectious lymphocytosis, a clinical entity featured by a benign relative and absolute increase in the number of small mature lymphocytes, was first described in 1941 by Smith.¹ He presented 2 cases of this disease and expressed the opinion that the group of patients reported by Reversbach and Lenert² and 1 case described by Wilson and Cunningham³ belonged in this classification rather than among the cases of infectious mononucleosis, as reported. There were no significant clinical signs or symptoms in any of these cases. Another case of acute infectious lymphocytosis presenting a marked symptomatology has been described,⁴ and the belief was expressed that 2 of the cases reported by Thelander and Shaw⁵ as infectious mononucleosis should be classified as acute infectious lymphocytosis. Smith⁶ has recently summarized his experience with acute infectious lymphocytosis and has described 4 additional cases.

To date, all reported cases of acute infectious lymphocytosis have occurred in children under the age of nine. It seemed of interest, therefore, to present 2 cases in young adults.

CASE 1. A 20-year-old soldier was admitted to the station hospital on August 25, 1943. Rubella and epidemic parotitis had occurred in childhood. Otherwise, the past history was not significant. The family history was noncontributory.

For 1 week prior to admission, the patient had a "cold," accompanied by intermittent pains in the back and chest. Additional complaints of stomach cramps, headache and a mild, nonproductive cough eventually developed, fever was demonstrable and the patient was hospitalized.

The temperature on admission was 102°F. Physical examination revealed a slender, well developed young adult appearing neither acutely nor chronically ill. The throat was mildly inflamed, and there was a small collection of mucus in the posterior pharynx. A small, tender lymph node was palpable in the right submaxillary region. The remainder of the examination was normal.

The symptoms completely disappeared within a few hours after admission, but during the first 2 weeks of hospitalization the temperature was elevated each morning to from 99 to 101°F, dropping to normal each afternoon or early evening. On August 30 there appeared a generalized morbilliform rash, which gradually faded and disappeared 4 days after onset. With its disappearance, a few small, nontender, axillary and inguinal lymph nodes became palpable. One week later, these were no longer felt. On September 13, the afternoon temperature was 100.2°F, rising to 104°F the following day. There was then a rapid fall in the temperature, but the patient continued to run a low-grade fever every morning until discharged on September 27.

Agglutination reactions for *Eberthella typhosa*, *Salmonella paratyphi*, *Salmonella schottmülleri* and *Brucella abortus* and the Weil-Felix reaction were negative. A roentgenogram of the chest showed no abnormalities. Repeated examination of the urine gave results within normal limits. The Kahn reaction was negative. The electrocardiograph recorded normal tracings. Heterophil agglutination tests on September 5 and 13 gave negative reactions.

There was a moderate relative and absolute increase in the number of lymphocytes of approximately 2 weeks' duration (Table 1). Its onset occurred during the 1st week, the white-cell count, which had been normal on admission, increasing to 27,850 by the 7th day. Frequent examination of stained smears failed to reveal abnormal or atypical lympho-

cytes. Small mature lymphocytes accounted for the lymphocytosis. The proportion of large mononuclear cells never exceeded 5 per cent. Repeated determinations of the erythrocyte

TABLE 1 White-Cell and Lymphocyte Counts in Case 1

DATE	WHITE CELL COUNT	LYMPHOCYTES			
		SMALL %	LARGE %	TOTAL %	LYMPHOCYTE COUNT
8/26	6 400				
9/2	28 000	83	1	84	24 000
9/3	20 000	77	3	82	16 000
9/4	14 000	76	5	76	11 000
9/5	18 000	60	3	63	12 000
9/6	19 000	77	4	81	15 000
9/8	13 050	77	2	77	10 000
9/11	10 000	57	2	59	5 700
9/15	12 000	46	2	48	5 800
9/21	8 700	37	4	41	3 600

and total polymorphonuclear-cell counts and hemoglobin content were within normal limits. Platelets were always present in the smear in adequate numbers.

CASE 2. A 19-year-old soldier was hospitalized on January 25, 1944. The family and past histories were noncontributory. The patient recalled epidemic parotitis, pertussis and varicella during childhood.

During the day preceding admission, the patient had noted a slight fever, a mild nonproductive cough, frontal headache and nasal obstruction. He was well developed and well nourished. A slight hyperemia of the conjunctivas, nasal mucosa and pharynx was the only abnormal finding observed on physical examination. The temperature on admission was 99.4°F, but thereafter was normal. The patient became asymptomatic 24 hours following hospitalization. Signs of the mild upper respiratory infection persisted for 4 days. Lymph nodes of significant size were never palpable.

A culture of the throat yielded *Staphylococcus albus* and a few pneumococci. A roentgenogram of the chest revealed no abnormalities. Urinalysis gave results within normal limits. The Kahn reaction was negative. Examination of the spinal fluid on January 28 was negative except for a cell count of 40, 40 per cent of which were lymphocytes and 60 per cent polymorphonuclear leukocytes. Re-examination of the spinal fluid on February 5 showed that the cells had dropped to 2 polymorphonuclear leukocytes per cubic millimeter. Heterophil agglutination tests on January 28 and February 5 and 15 gave negative reactions.

A moderate lymphocytosis caused by small mature lymphocytes was likewise present in this patient (Table 2), it was

TABLE 2 White-Cell and Lymphocyte Counts in Case 2

DATE	WHITE CELL COUNT	LYMPHOCYTES			
		SMALL %	LARGE %	TOTAL %	LYMPHOCYTE COUNT
1/25	22 000	65	2	67	15 000
1/26	15 000	63	3	66	10 000
1/27	20 000	65	3	70	14 000
1/28	22 000	55	3	60	13 000
1/29	16 000	64	2	66	11 000
1/30	12 000	62	3	65	7 800
1/31	13 000	68	3	73	9 500
2/1	14 000	57	3	62	8 700
2/2	15 000	58	3	63	9 500
2/3	9 500	38	6	44	4 100
2/4	11 000	40	5	45	5 000
2/5	8 700	37	4	41	3 400
2/6	14 000	31	5	36	5 000
2/9	8 800	31	4	35	3 100
2/15	9 000	25	5	30	2 700
2/19	7 500	23	6	29	2 200

observed over a period of 2 weeks. The maximum white-cell count was 22,000. No immature or atypical lymphocytes were seen at any time. The proportion of large mononuclear cells did not exceed 6 per cent. The platelet count varied

from 225,000 to 315,000. Repeated determinations of the hemoglobin content and the number of red cells were normal. The total number of polymorphonuclear leukocytes was constantly within the normal range. The bleeding and clotting times of the blood were normal.

DISCUSSION

The evidence for the establishment of acute infectious lymphocytosis as a specific entity has recently been summarized by Smith.⁶ He differentiates it from infectious mononucleosis, acute lymphatic leukemia and other infections associated with a lymphocytosis in children. The reader is referred to his paper for a comprehensive discussion.

I have encountered one other, apparently rare, consideration in the differential diagnosis of an absolute lymphocytosis in children. A relative and absolute increase in the number of small mature lymphocytes was observed during the administration of sulfadiazine to a child with a purulent otitis media in whom the initial reaction of the blood was that of a polynucleosis. The extent of the lymphocytosis was similar to that experienced in acute infectious lymphocytosis in children, but the white-cell count promptly returned to normal following discontinuance of the drug.

Study of the present 2 cases of acute infectious lymphocytosis in adults indicates that the disease is closely similar to that observed in children. Both patients had clinical evidence of a mild upper-respiratory infection. In addition, Case 1 presented symptoms usually attributed to a mild infection of the influenzal type. Both had clinical courses similar to that noted in several of the children previously reported (Cases R S and E S⁶). The patient in Case 1 had a morbilliform rash lasting for four days during the first week of the disease. A rash of this type has not been previously encountered in acute infectious lymphocytosis. It was similar to the rash reported in 57 to 18.5 per cent of cases of infectious mononucleosis. An extremely irregular febrile reaction was observed in Case 1 throughout most of the period of hospitalization. Similar temperature curves were observed in 2 of the children with acute infectious lymphocytosis (Case E N⁴ and Case M S⁶).

As stated above, the spinal fluid early in the course of the disease in Case 2 contained 40 cells per cubic millimeter, only 40 per cent of which were lymphocytes. This finding was similar to that encountered in 2 children reported by Thelander and Shaw.⁵ Although these patients presented symptoms of meningitis and encephalitis, respectively, there were no signs or symptoms, except for headache, referable to the nervous system in Case 2. The spinal fluid has been examined in only 1 other case of this disease (Case M S⁶) and was found to be normal. One other child with acute infectious lymphocytosis presented symptoms compatible with neurologic involvement, but examination of the spinal fluid was not done.⁴ Smith⁹ has recently

encountered 2 children with acute infectious lymphocytosis in whom the clinical picture resembled that of poliomyelitis. Collectively, these cases indicate neurologic involvement in an appreciable percentage of reported cases of acute infectious lymphocytosis, and suggest that this disease be included in the differential diagnosis of patients presenting neurologic signs and symptoms in association with an acute febrile illness.

The duration of the absolute lymphocytosis in adults appears to be shorter than that observed in children. The latter usually have elevated lymphocyte counts for periods of three to five weeks, in contrast to the shorter intervals observed in the present adult cases. Likewise, the maximum leukocyte counts of 27,850 and 22,000 encountered in the present cases were well below the usual range of 40,000 to 110,000 in children. A leukocytosis of 18,600 encountered in an eight-year-old girl has been the only exception to this range in children (Case E S⁶). All other aspects of the hematologic picture in the present cases were similar to those previously described.

Infectious mononucleosis presents the greatest problem in the differential diagnosis of acute infectious lymphocytosis in adults. Although still to be considered, the other diseases discussed in the differential diagnosis of acute infectious lymphocytosis by Smith⁶ are not so frequently encountered in adults. From August 1, 1943, to August 1, 1944, 12 cases of a relative and absolute lymphocytosis were observed in this station hospital. The cases of acute infectious lymphocytosis were the only ones encountered up to February 5, 1944. Ten cases of infectious mononucleosis were observed during the following five-month period. Although histories were obtained of contact between several of the patients with infectious mononucleosis, there was no possible contact between the patients with the two diseases. In spite of certain similarities, careful clinical, hematologic and serologic study of these cases corroborated the factors of differentiation between infectious mononucleosis and acute infectious lymphocytosis stressed by Smith.⁶

Clinically, the patients with infectious mononucleosis were sicker and for a longer period than those described in detail in this paper. The symptomatology of the cases of infectious mononucleosis conformed to that described in recent reviews.^{7, 10} In most of the reported cases of acute infectious lymphocytosis, the clinical findings have been minimal or completely absent. It must be remembered, however, that there have been cases (Case E N⁴ and Case M S⁶) in which the clinical picture was that of an acute and severe illness. The 10 cases of infectious mononucleosis had a marked lymphadenopathy, which sharply demarcated them from the minimal amount or complete absence of lymph-node enlargement encountered in the 2 cases of acute infectious lymphocytosis.

The principal point in the differential diagnosis of these diseases was made by frequent examinations of the peripheral blood smear throughout the course of the maximum white-cell counts in both diseases were within the same range. Thus, the extent of the white-cell count in adults cannot be used as a point of difference between the two diseases as it is in children, in whom the leukocytosis in acute infectious lymphocytosis is much higher than it is in infectious mononucleosis. Although there was considerable variation in the number of large atypical mononuclear cells in the differential smear from day to day in the cases of infectious mononucleosis, they were always present in significant proportions (8 per cent or more). Repeated examinations of the peripheral blood smear in the cases of acute infectious lymphocytosis failed to reveal the presence of these large atypical mononuclear cells at any time. The lymphocytosis was due in its entirety to small, mature lymphocytes. Although not sharply differentiated, the period of absolute lymphocytosis in the cases of infectious mononucleosis tended to be shorter—five to twelve days—than that encountered in the cases of acute infectious lymphocytosis, although it is well known that in the former the lymphocytosis may continue for months. Most of the cases of infectious mononucleosis showed a rather persistent relative lymphocytosis, with the continued presence of large atypical mononuclear cells, whereas the cases of acute infectious lymphocytosis returned promptly to a normal differential once the period of the absolute lymphocytosis had been completed.

The heterophil agglutination reaction has been uniformly negative in all cases of acute infectious lymphocytosis. In a recently reported series of 143 cases of infectious mononucleosis, the reaction was positive in significant titers (1:64 or higher) in 83 per cent.⁷ Nine of the 10 patients with infectious mononucleosis in the present study had titers of 1:64 or higher. The remaining patient, who presented typical hematologic findings, had a maximum titer of 1:28. Therefore the heterophil

agglutination reaction appears to be a negative laboratory test of considerable importance in the differential diagnosis of acute infectious lymphocytosis.

A review of the present literature on acute infectious lymphocytosis suggests that this disease is infrequently encountered. It is obvious that, with the minimal and varied clinical findings of many of the reported cases, the diagnosis of this disease will be missed unless a hematologic study is routinely accomplished. On the other hand, a more widespread familiarity with the varied manifestations of acute infectious lymphocytosis will result in its detection in a frequency greater than the reported cases indicate.

SUMMARY

Two cases of acute infectious lymphocytosis occurring in young adults are reported. The hematologic findings were similar to those previously recorded in children except that the extent of the lymphocytosis was less and its duration was shorter. A morbilliform rash was present for four days in Case 1, a finding not previously described in this disease. Changes in the spinal fluid were observed in Case 2, without clinical evidence of involvement of the nervous system.

The clinical, hematologic and serologic findings in these cases are compared with those in 10 cases of infectious mononucleosis.

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CLINICAL NOTE

PEDICULOSIS CORPORIS AND LEG
ULCERS*

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WHEN a middle-aged patient confronts a physician with ulcers of the legs for diagnosis and treatment, immediately such causes as venous



FIGURE 1

stasis, late spirochetal infection, cancer, erythema induratum, tuberculosis, sickle-cell disease, ecthyma, trauma, diabetes and self-infliction are considered. The dermatologist if consulted thinks also of deep mycologic infection, — blastomycosis, sporotrichosis, actinomycosis and so forth, — phagedenic ulcers, microaerophilic hemolytic strepto-

coccus infections, drug (especially halogen) ingestion, leprosy, mycosis fungoides, necrobiosis lipodica diabeticorum, scleroderma, leishmaniasis, cutaneous diphtheria, flea bites and tropical ulcers. To this list should be added the bites of the body louse, with the resultant scratching, infection and ulceration. In a large hospital clinic, ulcers of the legs due to pediculosis corporis rank second in frequency only to the so-called "stasis" (varicose) ulcers.

Several excellent textbooks on dermatology¹⁻⁴ fail to mention such ulcerations in the discussion of either pediculosis or ulcers. Other textbooks^{5,6} mention that ulcerations may occur but fail to stress adequately their occurrence on the legs. Thus, it is good practice to examine the entire body and clothing of patients with unexplained ulcers of the legs.

The ulcers are usually bilateral and multiple, and are most numerous on the lower third of the leg (Fig 1). They are shallow, oval or rounded (but may occasionally have straight sides), and generally ooze a syrupy fluid. They are ordinarily surrounded by an area of erythema. The legs frequently show localized hemorrhagic scratch marks, but the typical parallel linear scratch marks of pediculosis corporis are not usually present.

Such lesions respond well to eradication of the body lice, followed by the local application on alternate days of a 1 per cent aqueous solution of gentian violet and 2 per cent allantoin in a water-soluble emulsion base.

SUMMARY

Multiple ulcers of the legs are frequently due to infestation of the clothing with body lice. Search for such parasites should be made in all suspicious cases.

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MEDICAL PROGRESS

MYCOTIC INFECTIONS (Concluded)*

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SYSTEMIC MYCOSES

Included in this category are diseases caused by a wide variety of fungi, each of which may invade any tissue of the body, producing widespread infection resulting in death. These fungi induce a granulomatous type of infection, and differential diagnosis must include tuberculosis, syphilis, granulomas and neoplasms

Coccidioidomycosis

This is a highly infectious disease caused by *Coccidioides immitis* that produces a high incidence of infection, as shown by positive skin tests with coccidioidin, among native populations in the endemic areas of the San Joaquin Valley in California, around Phoenix and Tucson in Arizona and around San Angelo in central western Texas. Scattered cases have been reported from other areas in the United States, but most of them can be traced back to the localities mentioned above. A few cases have been reported from outside the United States, namely, South America, the Hawaiian Islands and Italy.

The fungus appears in the sputum, exudates and tissues as a large, single-celled, thick-walled spherule that reproduces by endosporulation. In culture, the fungus grows as a filamentous mold and reproduces by means of arthrospores, spores produced by fragmentation of its filaments.

Coccidioidomycosis is recognized as a pulmonary infection contracted by inhalation of the arthrospores of the fungus in dust, it simulates tuberculosis in all its clinical manifestations. The disease is divided into an acute primary infection of the lungs, usually followed by complete recovery, and a chronic progressive secondary granulomatous infection with a mortality rate of approximately 50 per cent.

The acute primary infection, with an incubation period of eight to fourteen days, simulates a cold, "flu" or bronchopneumonia. The symptoms may be mild or range in severity to severe prostration with chills, fever, malaise, anorexia, night sweats, headache, backache, pleurisy and rapid loss of weight. Physical signs in the chest are usually absent, and the x-ray films may be clear or may be indistinguishable from those of primary tuber-

culosis. Such an x-ray picture of the lungs clears rapidly, however. In about 2 to 5 per cent of such infections an associated hypersensitivity develops in five to fourteen days, manifested by erythema nodosum or erythema multiforme. Such skin lesions vary in duration from one to eight weeks, but the pigmentation may remain for months. Diagnosis is established by finding the large, nonbudding, endospore-filled spherules in the sputum, by culture and animal inoculation and by a skin test with 0.1 cc of a 1:1000 dilution of coccidioidin. Complement fixation and precipitin tests, using coccidioidin as the antigen, are useful diagnostic acids.

The chronic secondary progressive granulomatous infection is the result of an endogenous dissemination of the fungus either during the initial infection or later. Any organ of the body may be infected, and the symptoms are indistinguishable from those of tuberculosis. Demonstrating the organism is the only satisfactory means of establishing the diagnosis. Serologic (complement fixation and precipitation) tests are usually positive, but owing to the severity of the disease the patient may be anergic and give a negative skin test even with a 1:10 dilution of coccidioidin.

Treatment of the primary infection is symptomatic. Salicylates are helpful, but there is no specific treatment. Bed rest until the sedimentation rate and white-cell count are normal and until the lung findings, if any, show progressive clearing is all that can be accomplished. Recovery without sequelae should be expected.

Treatment of the secondary progressive infection is not satisfactory, and the mortality rate approaches 50 per cent. Many drugs have been used, but no consistent method of treatment has been established. Bed rest with a high-vitamin, high-calorie diet, as with tuberculosis, is advocated to support any resistance to the infection that the patient may have.

From 1894 to 1896, when Rixford⁸⁰ and Rixford and Gilchrist⁸¹ first described this infection in the United States, until 1936, the disease was known as coccidioidal granuloma and thought to be highly fatal. Gifford⁸² and Dickson,⁸³⁻⁸⁶ however, established the fact that a disease known locally in the San Joaquin Valley as "valley fever," "San Joaquin Valley fever," "desert fever" or "desert rheumatism" was a benign nonfatal form of coccidioidal granuloma not previously recognized.

Epidemiologic studies of this disease have shown that the fungus occurs in the soil,⁸⁷⁻⁸⁹ in wild ro-

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dents,^{90, 91} cattle and sheep⁹²⁻⁹⁷ and in dogs that have lived in endemic areas⁹⁸ The disease is acquired by inhalation of windblown dust laden with the spores of the saprophytic cultural form of *C. immitis* and not by a person to person or an animal to person transfer of the spherules found in the human or animal tissues during the disease⁹⁹

North American Blastomycosis

North American blastomycosis or Gilchrist's disease is a chronic infection caused by *Blastomyces dermatitidis*, with characteristic skin lesions and systemic involvement, particularly of the lungs, that is indistinguishable clinically from tuberculosis. The disease seems to be confined to the United States and Canada, since no adequately proved cases have been reported elsewhere.

B. dermatitidis appears in the sputum, exudates and tissues as a large, round, thick-walled, single budding organism. Cultured at incubator temperature, the fungus remains in the budding yeastlike parasitic form. Cultured at room temperature, however, the fungus develops a filamentous growth that reproduces by conidial formation from the sides of the filaments or from the ends of short branches.

In cutaneous blastomycosis the lesions occur on the exposed parts of the body, — face, neck, dorsum of hands, wrists and forearms, ankles and forelegs, — where they resemble the lesions of verrucous tuberculosis cutis or epitheliomas. Beginning as a papulopustule, such lesions slowly spread peripherally, break down to reveal a red granulating base covered with a dirty pink exudate and a raised papilliform or verrucous border with miliary-like abscesses. Occasional lesions seen in the genitoretal region should not be mistaken for granuloma inguinale. The clinical diagnosis is confirmed by demonstrating the large, round, thick-walled, single budding fungus in the exudate, crusts or pus from the peripheral miliary abscesses.

Systemic blastomycosis closely mimics tuberculosis. The fungus enters the body by way of the respiratory tract, and the lungs, skin and bones are the most frequently involved organs. Multiple subcutaneous gummalike nodules may appear anywhere on the body, and rupture to free a bloody pus. With widespread blood-stream dissemination of the fungus, the liver, spleen, kidneys and central nervous system are the usual sites of infection. The spleen and liver lesions are minimal, and the intestine is not invaded. Until skin involvement by subcutaneous abscess formation occurs, tuberculosis is the usual diagnosis. All attempts should be made, however, to find the fungus in the sputum or exudates when repeated examinations for the acid-fast tubercle bacillus are negative.

Treatment should not be started on any case of blastomycosis until an intracutaneous skin test with 0.1 cc. of heat-killed vaccine of the fungus has been done to determine the sensitivity of the patient to

the fungus or its products. Martin and Smith¹¹ have shown that lesions of patients sensitive to such materials rapidly spread when iodides or x-rays, or both, are used. Patients found not to be sensitive may be started immediately on potassium iodide by mouth or sodium iodide intravenously, whereas those patients who are sensitive should be given a course of desensitization before iodides are administered. Good results in the treatment of cutaneous blastomycosis should be expected. Results of the treatment of systemic blastomycosis depend on an early diagnosis and the immunologic status of the patient, as outlined by Conant et al.¹⁰¹

Since blastomycosis was described by Gilchrist¹² in 1896 and the fungus named *B. dermatitidis* by Gilchrist and Stokes¹⁰³ in 1898, several different fungi have been isolated from the disease and described as new genera or species. Comparative studies of these different fungi by Benham¹⁰⁴ and Conant¹⁰⁵ have shown them to be identical and the disease to be caused by a single etiologic agent.

The source of infection with *B. dermatitidis* has not been proved. Stober¹⁰⁶ isolated a white mold from the dwelling of a patient, but the fungus was not sufficiently described to prove it to be *B. dermatitidis*. Because of this report, it was thought that poor, unhygienic living conditions allowed contact with the fungus, which could be found in such places. There is evidence, also, that the fungus occurs in nature and that cutaneous blastomycosis is contracted by an introduction of the organism into the skin through abrasions or trauma. Toepel¹⁰⁷ reported a case following a thorn prick, and McKenty and Morgan¹⁰⁸ one from a scratch on the face. Robinson¹⁰⁹ described a patient whose onset followed a barefoot walk.

Ravogli,¹¹⁰ Werley¹¹¹ and Wohl¹¹² suggested the possibility that the disease was contracted from handling animals or their products, but failed to show the fungus in such materials. That animals do have the disease has been shown by Martin and Smith¹¹³ and Foshay and Madden¹¹⁴ in their reports of spontaneous infections in dogs. There has been, however, no proved transmission of the fungus from animal to man. The single transmission from man to man was reported by Evans¹¹⁵ in a physician who, at necropsy of a case of blastomycosis, cut his finger.

There seems to be no endemic area of the disease. Sporadic cases occur throughout the United States, and the lack or number of cases is an index only of the interest shown in the disease.

South American Blastomycosis

South American blastomycosis, paracoccidioides granuloma or Lutz-Splendore's disease is a chronic granulomatous disease of the mucous membranes of the mouth and regional lymph nodes, skin of the face and internal organs caused by *Paracoccidioides brasiliensis* or *P. cerebriformis*. The disease is largely confined to Brazil, but is reported occasionally from

her countries in South America, namely, Argentina, Paraguay, Peru and Venezuela

P. brasiliensis and *P. cerebriformis* appear in the exudates or scrapings from the lesions as large, round, multiple budding, thick-walled organisms. The buds, arranged around the periphery of the parent cells, may be as small as cocci (1 to 2 microns) or 30 microns in diameter. Cultured at incubator temperature these fungi develop yeastlike colonies not unlike those of *Blastomyces dermatitidis*. The multiple budding, parasitic tissue forms are found in such cultures. When cultured at room temperature, *P. brasiliensis* develops a filamentous colony that is cottony and *P. cerebriformis* develops a filamentous colony that is waxy, being smooth or wrinkled.

This disease has been divided into three distinct types — the mucocutaneous, the lymphangitic and the visceral. In the mucocutaneous type of infection, the portal of entry is the mouth, with ulcerating, vegetative, papillomatous lesions occurring on the buccal mucosa and spreading to the skin of the face around the mouth and nose. The regional lymphatics are invaded, and lymphatic invasion to the axillary, inguinal and other nodes of the body is not infrequent. Individual lesions around the mouth and nose are similar to those of mucocutaneous leishmaniasis and yaws, and a differential diagnosis can be obtained only by a laboratory study of material obtained from the lesions.

The lymphangitic type of infection is characterized by massive infection of the lymph nodes of the neck, with no external lesions until necrosis and drainage take place. The portal of entry is probably the mouth, with direct infection of the lymphoid tissue without mucosal lesions.

Visceral infection takes place through the intestinal tract, as evidenced by numerous lesions in the lymphoid tissues of the intestine. Massive infection of the lymph nodes throughout the viscera, enlargement of the spleen and liver and other organs and dissemination of the fungus throughout the body produce a highly fatal form of the disease.

Clinically, this disease differs from North American blastomycosis in that the portal of entry is the mouth, that the intestines are often infected and that in only 15 to 20 per cent of the cases are the lungs involved, in Gilchrist's disease the portal of entry is the respiratory tract or skin, the intestines are not infected and, in the systemic cases, 95 per cent have lung lesions.

Early reports from South America have stated that this disease is invariably fatal. Iodides have occasionally been employed with some success, but their use usually causes the lesions to spread. In view of the effect of iodides in hypersensitive cases of North American blastomycosis, the use of a desensitizing vaccine before iodide treatment in the South American disease seems indicated. Recent reports have shown that the sulfonamides give almost im-

mediate relief, with slow healing of the lesions. These drugs must be given in daily doses over long periods of time — in some cases as long as one to two years.

South American blastomycosis was described first in its cutaneous form by Lutz¹¹⁶ and Carini¹¹⁷ in 1908. The first generalized infection was recognized by Splendore,¹¹⁸ who¹¹⁹ later named the fungus *Zymonema brasiliense*. For a period of years this fungus was thought to be identical with *Coccidioides immitis*.¹²⁰⁻¹²³ In 1930, however, Almeida¹²⁴ showed by comparative studies of material obtained from cases of coccidioidomycosis occurring in the United States and material obtained from Brazilian cases that the two diseases were different. He named the South American fungus *P. brasiliensis*. The cases of coccidioidomycosis reported from South America, therefore, were cases of blastomycosis caused by the multiple-budding *Paracoccidioides* that had been mistaken for the nonbudding, endospore-forming coccidioides. Only three cases of coccidioidomycosis have occurred in South America. Posadas¹²⁵ described the disease from Buenos Aires in 1892 but failed to name the fungus. Fonseca¹²¹ reported a case from the Chaco of Argentina in 1928 but named the fungus *Pseudococcidioides mazzai*, and Negroni and Villafane Lastra¹²⁶ reported a case from Serrezeuela, Province of Cordoba, also in Argentina, in 1939, but named the fungus *Trichosporon proteolyticum*.

The South American disease is said to be caused by three distinct species of *Paracoccidioides* — *P. brasiliensis* (Almeida¹²⁴), *P. cerebriformis* (Moore¹²⁷) and *P. tenuis* (Moore¹²⁸). Several investigators,¹²⁹⁻¹³¹ however, would reduce these species to synonymy, and Conant and Howell¹³² would place them all in the genus *Blastomyces* as a single species, *B. brasiliensis*.

Cryptococcosis

Cryptococcosis (European blastomycosis, Busse-Buschke's disease, torulosis or *Torula meningitis*) is a subacute or chronic granulomatous infection of man and animals caused by *Cryptococcus neoformans*. This disease may be divided into cutaneous and systemic forms of infection, with the latter always terminating in meningitis because of the marked predilection of the fungus for nervous tissue.

C. neoformans appears in tissue, exudates, sputum and spinal fluid as a large, round, thick-walled budding organism surrounded by a thick capsule. In culture, at any temperature, the fungus remains yeastlike, mucoid, glistening and tan to dark brown. The same type of budding cells with wide capsules are found in cultures as in material from lesions.

Cutaneous cryptococcosis is characterized by acneform pustules that may ulcerate, granuloma-like ulcers, subcutaneous tumors or deep-seated abscesses that may develop anywhere on the body — cheek, neck, abdomen, thigh and groin. Such lesions are usually followed by cerebrospinal involvement or a generalized infection.

Infection of the central nervous system is characterized by protean clinical symptoms — headache, dizziness or faintness, convulsions, nausea and vomiting and signs of increased meningeal irritation with stiffness of the neck and positive Kernig and Brudzinski signs. The spinal-fluid pressure is increased, the cell count is high, and the globulin and albumin are increased, but the sugar content is low. A differential diagnosis would include tuberculous meningitis, syphilis, encephalitis, brain abscess, brain tumor and central-nervous-system degeneration.

Lung infections resemble tuberculosis or a neoplasm by x-ray examination, and diagnosis can be made only by finding the fungus in the sputum by direct examination or by culture.

India-ink preparations of gummy, blood-stained exudates from subcutaneous tumors, abscesses or ulcerations and sputum and wet Giemsa stains of frozen sections provide the best means of demonstrating *C. neoformans* in such materials. The spinal fluid should be centrifuged, and the sediment examined by the India-ink method. Such examinations reveal the round, thick-walled budding fungus surrounded by its characteristic and diagnostic wide gelatinous capsule.

Treatment of cutaneous cryptococcosis has not been too successful, and the disease usually terminates fatally with meningitis. Kessel and Holtzworth¹³³ reported a successful cure by oral iodides and x-ray treatment to individual lesions on the right and left breasts and amputation of a leg with a knee lesion that failed to heal. Dienst¹³⁴ reported a cure after oral iodides and x-ray treatment of a subcutaneous tumor attached to the tenth rib on the right side.

Central-nervous-system cryptococcosis has had a high mortality, not only because the diagnosis has not always been readily apparent, but also because there seemed to be no specific drug. Recent reports, however, have shown that the sulfonamides may be effective. Reeves, Butt and Hammack¹³⁵ reported recovery after treatment with sulfapyridine, and Marshall and Teed¹³⁶ reported recovery of a patient after treatment with sulfadiazine. Conant et al.¹³⁷ have reported a cure of a lung infection after sulfadiazine administration. These reports are a contradiction to the in-vitro studies of Keeney et al.¹³⁸ in which sodium sulfathiazole, sodium sulfadiazine and sodium sulfamerazine showed no effect on the growth of *C. neoformans* in culture. What part penicillin will eventually play in the treatment of this disease can be determined only after clinical trial. Keeney et al.¹³⁹ report no effect on the fungus in vitro, but Dawson et al.¹⁴⁰ report a killing effect comparable to that of *Staphylococcus aureus*. Jones and Klinck,¹⁴¹ however, have reported a case in which both sodium sulfadiazine and penicillin were of no value. Also, in-vitro experiments with cultures and in-vivo experiments with mice showed both these drugs to have no effect.

That cryptococcosis as it occurs in this country is the same as Busse-Buschke's disease¹⁴² (European blastomycosis) cannot be doubted, since Benham¹⁴⁴ showed the identity of the etiologic agents. The disease is world-wide in distribution, and the fungus is the same regardless of the type of case from which it is isolated.

C. neoformans was first isolated under natural conditions from peaches by Sanfelice.¹⁴⁵ It has been isolated from animals. Sanfelice¹⁴⁶⁻¹⁴⁷ obtained *S. lithogenes* from an ox and *S. granulomatogenes* from swine, Frothingham¹⁴⁸ *Torula* sp. from a horse, Harrison¹⁴⁹ *T. nasalis* from a horse, and Weidman and Ratcliffe¹⁵⁰ *T. histolytica* from a cheetah. Although the fungus has been isolated from nature and animals, there have been no reports of a natural infection or of transmission from animal to man. The portal of entry in man is thought to be the skin, respiratory tract or intestinal tract. Weis,¹⁵¹ who compared *C. neoformans* with a species of *Blastomyces* (*T. klein*) isolated from milk by Klein,¹⁵² suggests that the intestine can, at times, be the portal of entry.

Histoplasmosis

Histoplasmosis (Darling's disease or reticuloendothelial cytomycosis) is an infection of the endothelial cells of the reticuloendothelial system by *Histoplasma capsulatum*. Because of the intracellular distribution of the fungus throughout the body by such a system, the organism resembles *Leishmania donovani* and the disease resembles kala-azar.

H. capsulatum appears in the mononuclear or polymorphonuclear cells of peripheral blood smears, sternal bone-marrow smears, splenic-pulp smears and in tissue sections as a small, oval, sometimes budding cell 1 to 5 microns in diameter. Cultures of such materials on blood agar at incubator temperature develop the small, budding, yeastlike cells. Cultures grown at room temperature, however, develop a filamentous moldlike colony, which may be identified by the characteristic large tuberculate chlamydospores produced from the filaments.

Darling's original description of the disease stated that fever, anemia, leukopenia, splenomegaly, hepatomegaly and emaciation were the outstanding symptoms. Such symptoms may also be those of kala-azar. With the increasing number of cases described within the past few years, it has become evident that the symptomatology varies considerably. Marked lymphadenopathy may necessitate a differential diagnosis to include Hodgkin's disease, lymphosarcoma and aplastic anemia. Many patients have shown ulceration of the tongue, pharynx or larynx and ulceration of the mucosa of the nose that might be mistaken for carcinoma. Several types of skin lesions have been described — papular eruptions, deep punched-out ulcers, petechial hemorrhages and bullous lesions. In the lungs, the parenchymal changes and scattered miliary

esions may be typical of tuberculosis. Symptoms referable to the intestinal tract are diarrhea, hemorrhage and vomiting, with frequent ulceration of the lymphoid tissue found at autopsy.

Treatment of this disease has not been successful in spite of the use of a wide variety of drugs.¹⁵³

Histoplasmosis was first described by Darling¹⁵⁴⁻¹⁵⁶ from the Canal Zone and considered to be a tropical disease caused by a protozoan, *H. capsulatum*, closely related to the Leishman-Donovan bodies reported in cases of kala-azar. Rocha-Lima¹⁵⁷ reported the occurrence of budding by these organisms and hence considered them to be a fungus, *Cryptococcus*. Hansmann and Schenken^{158, 159} in 1933 and 1934 and DeMonbreun¹⁶⁰ in 1934 were able to culture the organism and definitely proved that it was a fungus. Since then, numerous cases have been described, showing the disease to have a world-wide temperate and subtropical distribution, with the majority of cases occurring within the United States. Meleney¹⁶¹ reviewed 32 cases up to 1940, and at the present time 74 cases have been reported. The recent excellent review by Parsons and Zarafonetis¹⁵³ discusses 71 of these. In this publication may be found the best discussion of the disease to date.

Actinomycosis

Actinomycosis is a chronic suppurative, purulo-granulomatous type of infection characterized by the formation of multiple draining sinuses and caused by a single anaerobic species of *Actinomyces*, *A. bovis*, and several aerobic species of *Nocardia* (*Actinomyces*).

Such fungi appear in the tissues, sinus walls or pus as macroscopic granules, which may be yellowish-white, red or black. Microscopically, these granules are composed of a tangled mass of delicate (1 micron in diameter) branching filaments, which are sometimes terminated at the periphery of the granule by broad sheaths, giving the appearance of clubs. When stained by Gram's method, the filaments are gram-positive, and the sheaths, gram-negative, in some species the filaments are also acid-fast.

Cervicofacial actinomycosis, caused by *A. bovis*, is probably the most frequent clinical type of the disease. There is usually a previous history of tooth extraction or infection referable to the teeth followed, after varying periods of time, by a direct extension of an infection through the tissues of the lower jaw and neck. Extensive cellular infiltration of the lesion produces a tumor-like hard mass, from which abscesses rupture, leaving multiple draining sinuses. The sanguinopurulent pus draining from such sinuses contains the characteristic granules. Occasional extension of the infection to the cranial cavity results in brain abscesses.

Pulmonary actinomycosis is characterized by the chronicity of the infection, often with minimal symptoms. Cough, low-grade fever, malaise and

loss of weight are the usual findings. X-ray films of the lungs may be typical of tuberculosis with apical lesions or may suggest neoplasm with a hilar mass, but usually the infection is confined to the lower half of the lungs. Involvement of the pleura with effusion, adhesions and thickening is often found in advanced cases. The ribs are frequently invaded. The diagnosis may not become apparent until direct extension of the infection to the thoracic wall produces abscess formation and draining sinuses, from which the granules are recovered.

Metastatic cerebral abscesses or meningitis is a frequent complication of primary lung infection. Actinomycosis of the central nervous system usually does not present symptoms referable to a distinct clinical entity. Spontaneous remissions, however, are more frequent in this disease than in those caused by bacteria.

Abdominal actinomycosis usually originates in the region of the appendix and cecum, presenting the picture of subacute appendicitis. Often the disease follows appendectomy, with failure of the scar to heal completely or a breaking through of a sinus in the old scar or in the region of the navel. Irregular tender abdominal masses may be felt, the viscera usually become infected, as do the vertebral bodies of the spinal column. Until a sinus or sinuses appear in the abdominal wall or groin that drain pus containing the granules, these abdominal lesions present difficult diagnostic problems.

Actinomycotic infections of the limbs (mycetoma) are caused by aerobic species of *Nocardia* (*Actinomyces*). The infected foot, knee, hand or arm becomes swollen and deformed, with abscess formation and draining sinuses appearing throughout the mass. In this type of infection the granules may be colored (red or black) in contrast to the sulfur-colored granule of *A. bovis*. Several species may cause such a disease — *N. asteroides*, *N. brasiliensis*, *N. mexicana*, *N. madurae*, *N. paraguayensis* and *N. pelletieri*. These species are identified by their reactions on milk, gelatin, serum and tyrosinase agar, type of growth on Czapek's agar and Sabouraud's agar, production of pigment, odor and, finally, their microscopic morphology and staining reactions (some are acid-fast). *N. asteroides* has been isolated not only from mycetoma but also from cases of diffuse peritonitis, of pseudotuberculosis with cerebrospinal meningitis and of brain abscess.

Treatment of actinomycosis by adequate surgical drainage combined with x-ray therapy and iodides has proved successful, particularly in cervicofacial infections. With the advent of sulfonamides and penicillin, more specific drugs may now be used with surgical drainage to combat the more difficult thoracic and abdominal cases. The sulfonamides and penicillin may act only against secondary bacterial infections and allow more radical surgery. Cutting and Gebhardt,¹⁶² however, showed sulfathiazole and

sulfadiazine to have some inhibiting effect on the growth of *A. hominis*. Benbow, Smith and Grimson¹⁶³ reported excellent results with sulfadiazine and iodides in pulmonary actinomycosis caused by *N. asteroides*. Keeney et al.¹²⁰ have shown penicillin to be effective against *A. bovis* in culture.

Cultures should be attempted in every case to determine the type of infecting fungus, aerobic or anaerobic. Cultivation of infected materials on common bacteriologic media and Sabouraud's agar is sufficient to isolate the aerobic species. The anaerobic *A. bovis*, however, can be isolated only by more exacting methods. Rosebury, Epps and Clark¹⁶⁴ used brain-heart-infusion agar plates, to allow streaking and subsequent picking of well isolated colonies. Such plates were incubated in anaerobic jars in the presence of 5 per cent carbon dioxide. Although shake agar cultures, chopped-meat medium and dextrose broth may also be used successfully with uncontaminated materials, the above method of culture is superior when contaminants are present.

The source of infection with *A. bovis* is endogenous. Several reports of the cultivation of this fungus from tonsillar crypts and carious teeth have established the human mouth as the habitat of this anaerobic species.¹⁶⁶⁻¹⁷⁴ Gordan and Hagan¹⁷⁵ were able to cultivate aerobic acid-fast *Nocardia* (*Actinomyces*) from soil samples and to show one to be pathogenic for rabbits. The pathogenic aerobic species, therefore, probably occur in the soil and are introduced into the body through the skin (mycetoma) or through the respiratory tract or intestine (systemic).

Moniliasis

Of all the mycotic infections, moniliasis is the most difficult to prove by clinical or laboratory methods. Species of the genus *Candida* (*Monilia*) have been isolated from normal mouths,¹⁷⁶ normal intestinal tracts,¹⁷⁷⁻¹⁷⁸ the vagina¹⁷⁹⁻¹⁸⁰ and the skin.¹⁷⁷ Such fungi can be found in the sputum of recognized pulmonary diseases, such as tuberculosis and carcinoma. They are also found in the stools from diseases in which diarrhea is a symptom, such as sprue¹⁸¹ and pernicious anemia.¹⁸² The prevalence of these fungi in normal conditions and diseases in which other etiologic agents are known to be the cause makes the diagnosis of moniliasis possible only by exclusion.

Species of *Candida* appear in clinical materials as small, oval budding cells with occasional mycelial elements. They are gram-positive when stained by Gram's method. In culture on Sabouraud's medium they develop smooth, white, yeast-like colonies, with oval budding cells on the surface and a mycelium penetrating the agar. Such cultures have a distinct yeasty odor. Only a single species, *Candida* (*Monilia*) *albicans*, is pathogenic.

C. albicans may be the primary cause of disease in a number of clinically recognized conditions. Thrush,

or infection of the mucous membranes of the mouth, is encountered more frequently in children than in adults. On the mucosa of the mouth are found extensive or scattered creamy white patches that reveal, on microscopic examination, the budding cells and mycelial elements of *Candida*.

Perlèche is an infection of the corners of the mouth characterized by macerated, eroded or fissured lesions from which *C. albicans* can be isolated. Such lesions, however, may be associated with a dietary deficiency, and the fungus, which can be found in normal mouths, may be a secondary contaminant.

Vulvovaginitis is a thrushlike infection of the vaginal mucosa and vulva characterized by irritation, pruritus and discharge. The fungus can be found in smears from the vagina and vulva or cultured from swabs used to collect material from the vagina. Pregnancy and diabetes are predisposing factors in the occurrence of this disease.

Infection of the skin by *C. albicans*, except in systemic infections, is usually confined to areas where closely approximating parts cause, with the aid of perspiration, mechanical irritation and maceration of the tissues. Intertrigo of the axillae, inguinal region and inframammary areas is characterized by erythematous, exudative lesions with sharply margined vesicular or papulosquamous borders. Obesity may be a predisposing factor aiding infection in all the mentioned areas, lactation a factor in the inframammary areas, and diabetes a factor in the intergluteal region. Intertriginous lesions are frequent in dishwashers and others who find it necessary to keep their hands immersed in water over long periods of time.

Onychia and paronychia are often caused by *C. albicans*, being characterized by thickened, grooved, sometimes discolored nails with painful paronychial swellings. Microscopic examination of scrapings in potassium hydroxide preparations reveals the budding yeastlike cells.

Bronchomoniliasis is characterized by a persistent cough, mucoid sputum with white flakes composed of cellular debris and yeastlike cells, a few scattered rales at the lung bases and x-ray films showing a slight to moderate peribronchial thickening. A more extensive invasion of the lungs, producing pulmonary moniliasis, is sometimes indistinguishable from tuberculosis. Malaise, fever, night sweats, chest pain, dyspnea, cough and hemoptysis, with signs of pleural thickening and consolidation, are not unusual. The disease may be acute, with rapid onset, or chronic, with frequent remissions and exacerbations.

Systemic infections are rare but do occur following prolonged refractory stomatitis, glossitis or resistant infections of the skin, particularly in the debilitated patient. Rockwood and Greenwood¹⁸³ and Miale¹⁸⁴ have reported 2 fatal cases, with autopsy findings. In Miale's case and another reported by

Smith and Sano,¹⁸⁵ the central nervous system was involved

Mycotic endocarditis caused by species of *Candida* have been reported in drug addicts by Joachim and Polayes¹⁸⁶ and Wikler and his associates.¹⁸⁷ These cases, however, yielded cultures of *C. parakrusei* and *C. guilliermondii*, two species considered to be non-pathogenic

The possible role of the yeastlike fungi in the pathogenesis of the diseases from which they had been isolated could not be determined until standard methods of classification allowed these organisms to be identified. Hundreds of species differing but slightly from each other have been reported in the medical literature, and until recently, attempts to classify them have resulted in confusion. Comparative studies of cultures by Benham,¹⁸⁸ Martin et al.,¹⁸⁹ Martin and Jones¹⁹⁰ and Langeron and Guerra¹⁹¹ have succeeded in reducing the vast number of reported species to a few well described organisms. These methods can be used to identify quickly and easily yeastlike organisms isolated from any infectious process. The reported incidence of a yeastlike fungus, if identified accurately according to these methods, now has meaning, and the previous confusion regarding their ability to cause disease should be lessened.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31321

PRESENTATION OF CASE

A thirty-one-year-old man was admitted to the hospital complaining of weakness, nausea and vomiting.

Five days before admission he slipped on the bottom step of a stairway, falling heavily on the left elbow and the left side of the thoracic cage. The patient's left ribs were strapped, and he was later sent to the emergency ward of this hospital, where he spent the night. The following morning he was fairly comfortable and was discharged. At home he did not feel well, complaining of profuse perspiration, of progressive weakness and of pain in the left thoracic cage. On the day before admission, malaise, nausea and intermittent vomiting appeared. On the day of admission the vomiting recurred. He complained of hiccoughs and of pain in the left upper quadrant of the abdomen and in the left shoulder.

The patient was well developed and well nourished, slightly icteric and in acute distress. The skin was cold and somewhat clammy. The heart and lungs were normal. The abdomen was soft, with no spasm or rebound tenderness, but there was tenderness in the left upper quadrant. There was no definite fluid wave or shifting dullness.

The temperature was 98°F, the pulse 100, and the respirations 25. The blood pressure was 110 systolic, 70 diastolic.

The red-cell count was 2,500,000, and the white-cell count 10,000. The icteric index was 15. A flat plate of the abdomen showed that the stomach was full of air. The splenic shadow was much larger than usual, and the lateral wall of the stomach was slightly serrated. There was no fracture of the ribs overlying the spleen. There were no dilated loops of bowel. Some gas was present in the sigmoid.

Soon after admission an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CARROLL MILLER. Several points in this patient's story are likely to be confusing to the first observers of such a case. The patient stressed a blow to the left side of the chest, and he had pain in that region. Naturally when an examiner sees such a

patient in the Emergency Ward or at home he thinks immediately of broken ribs, and the obvious treatment for such a condition is strapping to immobilize the broken parts. In addition to pain this patient had weakness, nausea and vomiting. Unless a person is relatively susceptible to pain, a blow in the lower chest does not cause these symptoms, and one must therefore think of other conditions to explain them. I should be interested to know if any blood studies were done when the patient first came into the Emergency Ward.

DR. BENJAMIN CASTLEMAN. None are recorded.

DR. MILLER. He apparently came into the Emergency Ward fairly soon after the accident. He felt reasonably comfortable the next morning and went home. Weakness persisted, however, and he complained of profuse perspiration. In the light of what must have been subsequently found we can explain these symptoms. He began to have malaise, nausea and vomiting. Then, as the condition progressed, he had hiccoughs and pain in the left upper quadrant of the abdomen — a slight shift downward from the chest — and in the left shoulder. When there is trauma to this part of the body one thinks first of injury to the spleen, of course, other viscera that may be injured in that region are the splenic flexure of the colon, the stomach and the kidney. We know that it takes a fairly severe blow to cause a rupture of a hollow viscus and also a reasonably severe blow to cause sufficient contusion or rupture of the kidney to produce symptoms in that region. It may, however, take only an extremely slight blow to cause a laceration or rupture of the spleen.

So far as physical signs are concerned, he must have been pale, although it does not say so in the account of the case. He was slightly icteric, cold, somewhat clammy and definitely sick. These signs go only with what might be called mild shock. The pulse was up a bit, and the blood pressure was perhaps slightly lower than that which a man of his age and condition should have. The positive findings on examination consisted mainly of tenderness in the left upper quadrant of the abdomen. There was no fluid wave or shifting dullness. The laboratory tests showed a marked reduction in the number of red cells, and the white cells were slightly elevated. The icteric index was definitely elevated. A flat plate of the abdomen in such a condition is of considerable interest, and I think that we might see the x-ray films at this point. In such films one should first attempt to demonstrate air under the diaphragm, indicating leakage from a hollow viscus, and then signs of fluid, although these are frequently not easily recognized in the ordinary flat film.

DR. MILFORD D. SCHULZ. The diaphragm is not shown on these films. I do not know whether there is air beneath it, but there certainly is no evidence of air in the peritoneal cavity. The stomach is full of air, and there is some serration of its lateral margin. The lower pole of the spleen is large and round.

*On leave of absence.

I cannot trace the splenic shadow upward I cannot see the edge of the liver I might point out that one femoral head is deformed

DR MILLER Apparently an old process?

DR SCHULZ Yes

DR MILLER Would you say that the splenic flexure of the colon is lower than usual?

DR SCHULZ I do not know I cannot see it

DR MILLER Another condition that I did not mention in association with intra-abdominal injuries is rupture of the liver, which is less likely with injury of the left side of the abdomen than it is with injury of the right side *Contrecoup* rupture, however, does occur

My presumptive diagnosis in this case is a delayed rupture of the spleen We have evidence for this both from the clinical findings and from the statistics reported in the literature There was an increase in the size of the splenic shadow Dr Schulz has pointed out the lower border of the spleen, but there seems to be further density medial to the spleen, pushing the stomach a little more to the midline than it ordinarily would be The course of events in this case is quite typical Immediate rupture of the spleen usually follows a fairly severe injury Late rupture may occur within a week and sometimes even later It is said that 50 per cent of the delayed ruptures take place within the first week and that an additional 25 per cent occur within a two-week period after injury

How can one explain a late rupture? Usually it is due to subcapsular contusion followed by breaking up of the splenic pulp, hemorrhage beneath the capsule and gradual stretching, with increasing tension of the capsule until the capsule breaks and releases both the accumulated and fresh blood There may be a rupture of the capsule at the time of the first injury, but because of certain clotting mechanisms, thrombi form in the region of the spleen, which seal off all the viscera locally, thus preventing spread into the rest of the abdomen No shifting dullness or free fluid in the abdomen was found on physical examination The icteric index may have been increased because of the absorption of hemoglobin from the peritoneal cavity or from spleen, which might have had an accumulation of hemolyzed blood within the splenic capsule There apparently was no intrathoracic disease, and no fluid was demonstrated either by physical or by x-ray examination There was no fracture of the ribs overlying the spleen Of course, one must always suspect fracture of the ribs, with puncture of the pleura and an accumulation of intrapleural blood, when there is a complaint of weakness and pain in the left side following an injury

I think that the important point, presuming my diagnosis to be correct, is that it is easy to skip over such a case lightly and to discharge the patient home, permitting him to carry on full activity after a few days We have had several cases within recent years

in which such an injury has been sustained, these patients have to be watched carefully for the development of symptoms It is important to remember that splenic rupture can occur late, and that when it does it may be one of the most acute abdominal emergencies that we see The patient must be operated on immediately, and even in case of doubt, an exploratory laparotomy is warranted

I shall close my discussion by saying that this patient had a traumatized spleen, probably a subcapsular contusion, at the time of injury, which about five days later ruptured into the peritoneal cavity producing nausea and vomiting, in other words, he had a delayed rupture of the spleen

I neglected to ask about a urinalysis at the time of admission

DR CASTLEMAN It was negative

Have you anything further to say about the x-ray films, Dr Sosman?

DR M C SOSMAN I should say that the patient had an enlarged spleen, which displaced the stomach upward and medially A ruptured spleen is a logical diagnosis, with hemorrhage into or around the spleen, or both

DR EDWARD HAMLIN, JR I saw this patient fifteen minutes before operation At that time he had definite shifting dullness At operation the spleen was four to five times its normal size It was soft and mushy and somewhat larger than one would expect from just intrasplenic hemorrhage It was easy to remove

DR CASTLEMAN Was there a large amount of free blood in the abdomen?

DR HAMLIN A great deal

CLINICAL DIAGNOSIS

Ruptured spleen

DR MILLER'S DIAGNOSIS

Delayed rupture of spleen

ANATOMICAL DIAGNOSES

Gaucher's disease.

Ruptured spleen

PATHOLOGICAL DISCUSSION

DR CASTLEMAN The spleen that we received weighed 800 gm and contained three tears—one on the upper pole, one on the medial surface and one on the posterior aspect The largest, the one on the medial surface, was 9 cm in length and 1 cm in depth The surface was otherwise smooth The cut surface was brick red except for several well circumscribed hemorrhagic areas, measuring 1 or 2 cm in diameter, scattered throughout the parenchyma, not necessarily close to the capsule We were not able to find any really large hematomas beneath the capsule We thought that it was an ab-

mal spleen but could not pin a definite diagnosis on it grossly. It did not look like a Banti spleen, and it was not hard enough, but it did suggest the spleen of hemolytic jaundice. Sections, however, showed the characteristic histologic picture of Gaucher's disease. Throughout the pulp there were numerous large foamy slightly granular cells with

canals of the femurs and humerus are widened at the expense of the cortices. The lower ends of the femurs show the Erlenmeyer-flask deformity, which is quite typical.

DR. CASTLEMAN: This disease usually occurs in young persons. This man was thirty-one, but it has been reported in people over fifty. I believe that a



FIGURE 1 Photomicrograph of Spleen Showing the Large Number of Gaucher Cells. Note the absence of Gaucher material in the endothelial cells lining the sinusoids.

small round pyknotic nuclei (Fig. 1). The follicles were reduced in number, owing to replacement by the Gaucher cells, which, as you may recall, are reticulum cells filled with kersatin,—one of the cerebrosides. The one clue to the diagnosis was in the x-ray film of the femoral head. Dr. Schulz, will you show the films taken after the diagnosis was established?

DR. SCHULZ: The films taken after operation show deformity of one femoral head. The medullary

large percentage of the cases have occurred in Jews, and this man was a Jew.

It is possible that these bone lesions, which are produced by the Gaucher cells within the marrow and not in the cortex, may increase in number. A number of cases have been reported in which bone lesions first appeared following splenectomy.*

This patient is doing well and is about to go home.

*Pick, L. Classification of diseases of lipid metabolism and Gaucher's disease. *Am. J. M. Sc.* 185:453-469, 1933.

CASE 31522

PRESENTATION OF CASE

First admission. A twenty-year-old housewife was admitted to the hospital complaining of abdominal pain and jaundice.

About nine months before admission the patient was referred to the Out Patient Department following one positive and one doubtful premarital Hinton test. Her fiancé was Hinton negative, and she admitted no other exposure. She denied having had any of the stigmas of acquired or congenital syphilis. The patient's mother and sister had had tuberculosis,

but there was no family history of syphilis or positive serologic tests. At that time, physical examination revealed nothing remarkable. Repeated Hinton tests were positive. One Wassermann test was positive, and another was questionable. A Wassermann test on the spinal fluid was negative. The patient was started on a course of antisyphilitic therapy. She had no ill effects from bismuth, but when Mapharsen was begun she complained of nausea without vomiting beginning about half an hour after each treatment and lasting for about two hours. She had no diarrhea or itching, and the stools and urine remained normal. Neoarsphenamine was

substituted for Mapharsen and caused some nausea until the dosage was reduced, after which there were no ill effects. While under treatment she had married, and six months before entry had become pregnant. Eight days before admission she ate some fried sea food and on the following day developed a constant sharp pain in the epigastrium and right upper quadrant. Nausea developed simultaneously with the pain, and was associated with a few episodes of vomiting dark-green material. Three days before admission the pain became severe and the skin and scleras were observed to be jaundiced. She developed constipation, her bowel movements having been normal until that time. The urine became dark. She felt feverish and had a temperature of 101 to 102°F. During the following three days the pain and jaundice subsided somewhat but the discomfort in the right upper quadrant remained.

Physical examination showed a well developed, well nourished, poorly hydrated, sick-appearing woman. The skin was hot and dry. A few blotchy red spots were observed over the face and palms of the hands. There was no definite jaundice, but the peripheries of the scleras had a questionable yellowish tint. The heart and lungs were not remarkable. The abdomen revealed moderate tenderness and slight spasm in the right upper quadrant. The upper margin of the liver was at the fifth rib, and the lower margin 5 cm. below the costal margin in the mid-clavicular line. Neither the spleen nor the gall bladder could be felt. The uterus was enlarged to occupy two thirds of the distance from the symphysis pubis to the umbilicus. Fetal motions and heart sounds were present. The pregnancy was estimated to be of six months' duration. Pelvic examination revealed moderate tenderness but was otherwise negative.

The temperature was 98.6°F, the pulse 100, and the respirations 22. The blood pressure was 118 systolic, 85 diastolic.

Examination of the blood showed a red-cell count of 4,310,000, with 10.5 gm. of hemoglobin, and a white-cell count of 19,300, with 80 per cent neutrophils. The urine had a specific gravity of 1.018, subsequently ranging from 1.002 to 1.014, the sediment contained 3 to 4 white cells per high-power field. The urine gave a positive test for urobilinogen in a dilution of 1:8. One week later it was present in a dilution of 1:64, and following this it was positive three times in a dilution of 1:16. The serum nonprotein nitrogen was 21.5 mg. per 100 cc., the phosphorus 2.6 mg., the protein 5.88 gm., the albumin 3.33 gm. and the globulin 2.55 gm. (an albumin-globulin ratio of 1:3), the alkaline phosphatase 4.2 Bodansky units, and the chloride 106 milliequivalents per liter. A bromsulfalein test (5 mg. per kilogram) showed retention of 60 per cent of the dye after forty-five minutes. A cephalin-flocculation test was negative in twenty-four hours but questionably positive after forty-eight hours. The van den Bergh test was

0.85 mg. direct and 1.2 mg. indirect. The prothrombin time was 17 seconds (normal, 18 to 20 seconds).

X-ray examination of the abdomen revealed a uterus enlarged to the third lumbar vertebra. The liver appeared normal in size. No gallstones were observed.

The patient was put on a high-carbohydrate, high-protein, low-fat diet. She was given vitamins intravenously and allowed fluids up to 2500 cc. per day. She received two injections of bismuth within the fourteen days following admission. The urinary sediment continued to show a few white cells. The red-cell count fell to 3,300,000. The blood pressure, temperature and pulse remained in a normal range. At that time, a cephalin-flocculation test gave a doubtful reaction after forty-eight hours and the van den Bergh test was reported as normal. The bismuth test was reported as normal. The liver was only 3 cm. below the costal margin and was much less tender than at first. The blotchy lesions on the hands and face improved, but the scleras remained "muddy." Bismuth injections were stopped, and a course of penicillin (1,200,000 units) was substituted.

On the nineteenth hospital day, following the injection of 1500 cc. of 10 per cent dextrose in water with the addition of nicotinamide, thiamine chloride, riboflavin, Hykinone and cevitamic acid, the patient complained of weakness and blurred yellow vision. There was edema of lids, as well as chemosis and large vitreous opacities in both eyes. She had a recurrence of the anorexia, malaise and slight liver tenderness. Her face became swollen and pale. These symptoms persisted. The fetus remained normal, with a strong heart beat at a rate of 144 per minute.

On the twenty-first hospital day the patient was discharged to a lying-in hospital. The blood pressure had risen from 130 systolic, 90 diastolic, to 150 systolic, 115 diastolic, and the urine gave a + test for albumin on the last two examinations.

Final admission (two weeks later). In the interim, labor had been induced at the lying-in hospital following the development of convulsions. She was delivered of a nonsyphilitic infant who lived only twenty hours. Following delivery, the patient developed fever, leukocytosis and pyuria. Two days before admission, she had a shaking chill, associated with a white-cell count of 50,000. On the day before admission she had one episode of vomiting.

On examination the patient was pale and thin. There were a few slightly erythematous lesions on the face. The eyes showed no residual chemosis. The fundi were pale but otherwise normal. The pharynx was slightly reddened and edematous. The heart and lungs were normal. The liver was tender and extended four fingerbreadths below the costal margin. There was no true spasm of the abdominal wall, but exquisite tenderness elicited in the right costovertebral angle. The uterus was well contracted.

The temperature was 105°F, the pulse 144, and the respirations 25. The blood pressure was 100 systolic, 65 diastolic. Examination of the blood showed a red-cell count of 2,550,000, with 7.5 gm of hemoglobin, and a white-cell count of 42,000, with 67 per cent mature neutrophils, 23 per cent band forms, 8 per cent lymphocytes, 1 per cent myelocytes and 1 per cent monocytes. The red cells were hypochromic and normocytic, with moderate variation in size and shape. The urine had a specific gravity of 1.007 and gave a +++ test for albumin, the sediment contained 2 to 3 red cells and innumerable white cells per high-power field. Culture revealed abundant colonies of colon bacillus. A stool gave a ++ guaiac test. The urine was positive for urobilinogen in a dilution of 1:32. The nonprotein nitrogen was 21.5 mg per 100 cc, the protein 5.95 gm, the albumin 3.52 gm, the globulin 2.43 gm, the chloride 100 milliequiv per liter, the van den Bergh normal, and the prothrombin time 29 seconds. Repeated Hinton tests were negative in all dilutions. The cephalin-flocculation test was negative after twenty-four hours and ++ after forty-eight hours.

The patient was put on a course of intensive vitamin and carbohydrate therapy. She was treated with small amounts of sulfadiazine. The temperature responded for a few days and then rose again to 104°F. She began to vomit frequently. The urinary intake and output were poor. The liver tenderness and costovertebral angle pain increased in severity. The liver became larger, and the abdomen became distended. Peristalsis could hardly be distinguished. There was shifting dullness, without definite fluid wave. The temperature spiked at least once a day, often rising to 104°F. Pelvic and rectal examinations were negative. X-ray examination revealed hepatomegaly and a suggestion of abdominal fluid.

On the eleventh hospital day the patient became mildly disoriented. She had a chill, and the temperature spiked to 104.8°F. On the thirteenth hospital day she complained of pain and exhibited tenderness in the right groin (femoral triangle), associated with rising temperature, pulse and respirations. On the seventeenth hospital day she had generalized convulsions and was momentarily unresponsive, the trachea filled with a coarse stringy exudate but soon cleared. On the nineteenth hospital day she became incontinent of feces. The pulse was rapid and threadlike, and the pharynx was full of hemorrhagic purulent material. The temperature was 104°F, and the respirations labored and slow. The latter rapidly became slower and then ceased altogether.

DIFFERENTIAL DIAGNOSIS

DR EARLE M. CHAPMAN. This is a long story of a young mother who died at the age of twenty. I

should like to go back and reconstruct the story from the beginning as I see it.

In the first place, on the evidence of a positive serologic test for syphilis she was treated with a highly toxic agent, arsenic. I am going to raise a doubt that she had syphilis because the story is not that of syphilis. There was no evidence physically of syphilis, and there were only these fluctuating tests to indicate such disease. I think that the work of Neurath and his associates* at Duke University differentiating positive and false-positive tests for syphilis has been a valuable contribution. Their method has been a great help to me recently in differentiating these cases. Strangely enough, three of my cases have been women in the same category as this. The reports were positive, but by the Neurath method they were shown to be biologically false. This patient we are discussing today, however, was treated with arsenic, and while under treatment, it seems to me that the liver was moderately damaged, not enough to explain her death. They looked vainly by means of repeated tests to determine whether the large and tender liver was sufficiently damaged to explain the outcome. The bromsulfalein test alone was positive, the first time it was done it showed retention of 60 per cent of the dye after forty-five minutes. The dose was quite large—5 mg per kilogram. The other tests indicated little damage. It is true that she had a slight degree of jaundice in the beginning, but this can be explained by a moderate arsenical hepatitis.

When we come to the present illness, we find that she had been perfectly well until eight days before admission, when she had abdominal pain, nausea, vomiting and fever, which are signs of acute infection. This sudden episode really is the clue, as I see it, to the cause of death. The record states that she had a rash on the face and hands. Of course that may be a red herring to make us believe that it was recurring secondary syphilis or it may hint that this was lupus erythematosus, but I see nothing in this illness to fit with either diagnosis.

What organ was the one that finally failed? I do not believe, as I have said, that the hepatitis was severe enough. None of the tests fit with cirrhosis of the liver. It is clear, however, that she had kidney trouble. The specific gravity was fixed, and she had albuminuria. The development of eclampsia with convulsions during pregnancy indicates that the kidneys had been damaged. Yet she came back to the hospital and died with a normal nonprotein nitrogen, which clearly shows that the cause of death was not uremia. Although she did not die of primary renal failure, she obviously had an infection in the urinary system.

On the second admission the urinary sediment contained numerous white cells and a culture yielded abundant colonies of colon bacilli. On physical

*Neurath H et al. Serological diagnosis of syphilis. *Science* 101:68, 1945.

examination she was edematous and had exquisite tenderness in the right costovertebral angle. She then continued to have evidence of infection, — I assume she had a septic type of temperature chart, — and she failed to respond to both sulfadiazine and penicillin. When a patient dies without responding to these, there is certainly one complication that has to be considered, namely, undrained pus. None of these chemotherapeutic agents will drain a septic area, that is a surgical procedure.

DR BENJAMIN CASTLEMAN You might like to glance at the temperature chart?

DR CHAPMAN It is just as I supposed, she certainly ran a septic course. Where was the sepsis located?

Going back again, I have to consider that the first attack may have been appendicitis, a frequent disease at this age, and therefore she may have had a pylephlebitis. But the one point that I believe is against pylephlebitis is the fact that the appearance of jaundice in five days favors an intrahepatic type of disease rather than an infectious process from a pylephlebitis. Of course, it may have originally been an inflammatory reaction of the right kidney, such as a perinephric abscess, causing a toxic picture with fever and failure to respond to chemotherapy. That would fit in with the final course, since she had exquisite tenderness in the right costovertebral angle.

There is one laboratory finding that is puzzling me and I cannot fit it into the picture, that is the ++ guaiac test in the stool. The excessively high white-cell counts and the anemia fit in with sepsis arising from pus in the right kidney on top of pyelonephritis, which she had had in a mild way previously, it having been linked with the eclampsia.

Now we come to the final phase of her illness. The history states that the liver increased in size, that the abdomen became distended and that peristalsis was minimal. There again, I think that we all know that kidney disease reflexly can simulate intestinal obstruction: the bowel becomes atonic secondary to renal disease, and that fits into the pattern. Then finally she had these convulsions and was unresponsive and hyperthermia was present — all of which leads one to think of some septic metastatic process in the brain, which I can see no possible way to diagnose.

DR CASTLEMAN Dr FitzHugh, you saw this patient. Will you tell us more about her?

DR GREENE FITZHUGH We believed that the blood picture and the albumin in the urine indicated a definite toxemia, and that is why we sent her to the lying-in hospital.

Two days after the pregnancy was interrupted, the blood pressure came down and the urine cleared, we then had quite a discussion whether we should give her bismuth, since she already had a damaged liver. At that time antisyphilitic treatment with penicillin had not reached the stage where it was

generally accepted. We had considerable discussion about the diagnosis. The syphilologists thought that it was syphilis and that we had better go on with some form of antisyphilitic therapy. So we started with bismuth, but with the reports that began to accumulate on the treatment of syphilis with penicillin, we decided that we could safely shift from bismuth to penicillin.

DR JOHN L. NEWELL When this patient was admitted to the Massachusetts General Hospital she was six months pregnant. I assume that she was recovering from toxic hepatitis, which was believed to have been caused by arsenical treatment. Then she developed a rather fulminating pre-eclampsia. We know that there is no better way to aggravate a pre-eclampsia than to have large amounts of fluid given intravenously.

I did not see her at the lying-in hospital, but she must have had a rapidly progressive course. I should say from an obstetric point of view that it was fortunate that they were able to induce her at seven months. They certainly did not operate. While at the lying-in hospital, she developed pyelitis, chills and eclampsia, which are commonly associated. In fact it is considered by some men that pyelitis is the etiologic agent. It seems to me that this might have been a pyelonephritis that had progressed to a perinephric abscess and the development of generalized sepsis.

CLINICAL DIAGNOSES

Toxic hepatitis
Pyelonephritis
Syphilis, latent

DR CHAPMAN'S DIAGNOSES

False-positive test for syphilis?
Arsenical hepatitis
Eclampsia, ante-partum
Pyelonephritis
Perinephric abscess
Septicemia
Brain abscess?

ANATOMICAL DIAGNOSES

Eclampsia
Infarcts of liver, multiple
Infarcts of spleen, kidneys, lungs, adrenal gland and brain
Septicemia, terminal (*Clostridium welchii*)
Septicemia (colon bacillus)
Multiple abscesses: abdominal wound, sternum, left clavicle, liver and adrenal glands
Focal necroses in liver
Pyelonephritis, acute

PATHOLOGICAL DISCUSSION

DR CASTLEMAN On the second admission to this hospital the clinicians were not sure of the diagnosis and decided to make a small incision to find

out what was wrong with the liver. They found an enlarged liver, a biopsy showed numerous areas of necrosis and hemorrhagic infarction in the periphery of the liver lobules, findings characteristic of eclampsia. Many of the vessels were thrombosed. In other words, she still had eclampsia when she returned from the living-in hospital. That, I believe, accounted for the large size of the liver and for all the liver symptoms. Following operation she did not do well, developed sepsis in the operative wound, from which we were able to culture colon bacilli, and died in about two weeks.

At autopsy the liver infarcts were widespread, there was thrombosis of the right hepatic artery, and microscopically thromboses were seen in many of the hepatic veins. The kidneys were tremendous in size, each weighing 350 gm., which is about twice the normal weight. There were numerous thrombi associated with hemorrhagic infarction, as well as old blood within the tubules. We also found tiny thrombi in the brain, with small foci of infarction. Just before she died she developed gas-bacillus infection, by the time we did the autopsy, eleven hours post mortem, gas bubbles were grossly visible and we were able to recover the Welch bacillus from every organ. I believe that was just a terminal event, since colon bacilli had been cultured from the blood before death. I think that we can explain the entire picture on eclampsia associated with a severe renal infection.

DR. CHAPMAN: What about the arsenic?

DR. CASTLEMAN: I do not know, I suppose that a liver previously damaged by arsenic may be more prone to develop eclampsia, although I do not recall ever having heard anything said about it.

DR. NEWELL: I have never heard that.

DR. CASTLEMAN: Of course, no one knows the cause of eclampsia. A toxic agent—whatever it is that starts it off—possibly causes more damage in a diseased liver than it does in a normal one.

DR. NEWELL: I am surprised that this patient apparently recovered clinically from the eclampsia and yet had all these manifestations.

DR. CASTLEMAN: Certainly the appearance of the liver is characteristic of eclampsia. Could it have been post-partum eclampsia?

DR. NEWELL: But she did not die post partum. Death occurred three weeks after the convulsions.

DR. CASTLEMAN: She had convulsions before delivery. Did she have any afterward?

DR. FITZHUGH: She had no post-partum convulsions in the living-in hospital. She had them before she was delivered and terminally at this hospital.

DR. NEWELL: Do you think that the terminal convulsions were due to eclampsia—after two and a half or three weeks?

DR. CASTLEMAN: I do not know. She had several small lesions in the brain. Certainly the changes in the kidneys and the liver and even in the heart are those that are usually found in eclampsia, but it is possible that they were the result of the original ante-partum eclampsia.

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MEDICAL CARE FOR VETERANS

THE failure of the people of the United States in the past to provide the best of medical care for veterans is inexcusable. It has been argued that such care should be limited to conditions or diseases directly or indirectly attributable to military service, but in many cases the line of distinction is difficult to draw and if there is any question the veteran certainly deserves the benefit of the doubt. Furthermore, it seems reasonable that medical and hospital care should be furnished for all veterans, without regard to the cause of their illnesses or disabilities. Now that thousands of wounded are being returned to this country, to be discharged to the care of the Veterans Administra-

tion after a certain period in Army and Navy hospitals, its facilities become of increasingly great importance, particularly since there is a possibility that the program will be extended to include the care of their dependents.

The Veterans Administration was created over twenty years ago, and in the intervening period, hundreds of millions of dollars have been turned over to it by Congress for the construction of hospitals, their staffing and their maintenance. In other words, the necessary wherewithal has been provided. Unfortunately, however, this type of medical practice has failed to attract the most competent of the medical profession.

Undoubtedly one of the reasons for this lack of appeal is the fact that physicians of the Veterans Administration are under the control and supervision of men with relatively little knowledge regarding medical matters. Three bills now before Congress (H. R. 3310 and 3317 and S. 1079) propose a department or bureau of medicine and surgery within the Veterans Administration.

Reorganization of the medical personnel along such lines would eliminate some of the difficulties of the past, but the provision that medical officers of the Army and Navy may be detailed for service in the Veterans Administration is an undemocratic maneuver that deserves little support. Rather than resort to compulsion, would it not be better to create a medical organization that appeals to the returning medical officer and to the recent graduate? Each hospital would have medical and surgical heads who are well known and competent in their particular lines of work. Appropriate salaries would be paid, and high-grade investigative work, carried out in well equipped and properly staffed laboratories, would be encouraged. In other words, these hospitals would be comparable with the modern first-class teaching hospital.

The advantages of a setup of this sort are obvious. In the first place the veteran would receive better medical care than he has ever received in the past. Secondly, medical research would be promoted. Thirdly, hospitals of this type would undoubtedly be approved for internships and residencies, and these facilities, in addition to being attractive to the recent medical graduate, would at

help considerably in the problem, as yet un-
 ed, of providing adequate means for the post-
 duate training of discharged medical officers
 d finally, the ultimate cost to the taxpayer — a
 tter that appears to receive little or no thought
 ase days — would be decreased

COSMETICS CONTAINING HORMONES

COSMETICS containing hormones are advertised
 tionally and are available everywhere for pur-
 ase without a prescription by a gullible public
 osmetics are defined as applications intended to
 eautify and improve the complexion, skin or hair
 hey are designed to make a person more attrac-
 ive, to delay (or perhaps better, to hide) the appear-
 nce of the manifestations on the skin of advanc-
 ng years, to cover defects and, in general, to make
 he skin softer and more pleasant to look on. The
 addition of hormones, which are physiologically
 active ingredients derived from endocrine glands
 or their synthetic duplicates, alters their status
 and creates a potentially serious situation. These
 beautifying preparations then become active and
 possibly dangerous and should be classed with cer-
 tain drugs, serums, vaccines, vitamins and other
 biologic products. As such they should come
 within the jurisdiction of the United States Pharma-
 copoeial Convention, the Committee on the Na-
 tional Formulary of the American Pharmaceutical
 Association or the Council on Pharmacy and Chemis-
 try of the American Medical Association. It is
 significant that none of these authorities have ac-
 cepted these hormone-containing preparations.

Extravagant claims are made of the glamorous
 results of such applications, and enormous sums of
 money in the aggregate are being spent by ill-
 advised people lured by such advertisements. There
 is, however, no satisfactory evidence that justifies
 the use of hormone-containing cosmetics for the
 purpose of local beautifying effects. The Federal
 Food and Drug Administration, as evidenced by
 a letter from Commissioner Dunbar published else-
 where in this issue of the *Journal*, is "skeptical of
 the benefits, if any, which accrue from the local use
 of these products." He adds, "We have con-

sistently informed manufacturers that because of
 the uncertainty of the ultimate effect of the use
 of these products and because of their dubious value
 we do not look with favor upon their distribution
 for lay use." On the other hand, sufficient absorp-
 tion from the injudicious use of estrogen-containing
 cosmetics to upset normal body activities has been
 demonstrated. Eller and Wolff* have recently re-
 viewed the evidence concerning the absorption of
 such preparations. In addition, the cancer-promot-
 ing properties of estrogenic substances are reason-
 ably well established. Much experimental work
 must be done to determine all the possible effects
 of a long-term use of such agents in the average
 human being, and pending such work, it is well that
 their use be carefully restricted.

The physician is seldom consulted regarding the
 use of cosmetics or their composition. He should,
 however, be cognizant of the fact that there is a
 lack of convincing data from carefully controlled
 studies to justify the lurid advertisements of the
 cosmetic manufacturers.

*Eller J J and Wolff S. Hormones and vitamins in cosmetics.
J A M A 114 1865-1875 and 2002-2010 1940

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

DEXTER — Fred F. Dexter, M.D., of Springfield, died
 on July 10. He was in his sixty-seventh year.

Dr. Dexter received his degree from Harvard Medical
 School in 1904. Before his retirement twelve years ago, he
 was a practicing gastroenterologist. He was secretary of the
 Eastern Hampden Medical Association from 1914 to 1915.
 He was a fellow of the American Medical Association and
 a member of the Springfield Academy of Medicine.

His widow survives.

DICKSON — Richard E. Dickson, M.D., of Holyoke,
 died on May 8. He was in his seventy-eighth year.

Dr. Dickson received his degree from Jefferson Medical
 College of Philadelphia in 1895. He had served as president
 of the Eastern Hampden Medical Association and was on
 the staff of the Holyoke Hospital. He was a fellow of the
 American Medical Association.

METCALF — Richard Metcalf, M.D., of Winthrop, died
 on May 21. He was in his fifty-eighth year.

Dr. Metcalf received his degree from Tufts College Medical
 School in 1913. He was a fellow of the American Medical
 Association.

His widow survives.

REDDY — Joseph W. Reddy, M.D., of South Boston,
 died recently. He was in his seventy-fifth year.

Dr. Reddy received his degree from Harvard Medical
 School in 1896 and retired from active practice in 1940. He
 was a fellow of the American Medical Association.

CORRESPONDENCE

PHYSICIANS FORUM

To the Editor Over the years preceding, during and following my incumbency as president of the Massachusetts Medical Society I have been disturbed by what has seemed to me the lack of opportunity for the minority (perhaps the majority) of the members of the Massachusetts Medical Society to present their point of view with a reasonable chance of its receiving appropriate attention. I feel that the same situation exists in the American Medical Association. In certain instances there have even been attempts to suppress the expression of opinion of the minority. How to correct this unfortunate situation has not been clear, but recently an opportunity to improve the situation seems to have developed due to the formation and growth of the Physicians Forum, Incorporated, for the study of medical care, of which I am an active member.

This organization started in New York City a few years ago among members of a county society of the New York Medical Society, who felt that there was need for a method of expressing the opinion of the minority in organized medicine. From its meager beginning it has become a national organization, and on December 8 and 9, 1944, held in Washington, D. C., a National Health Conference on the Problems of Medical Care, which turned out to be a meeting of real significance, with fifty-one organizations represented and many individuals of prominence participating.

The Forum analyzes relevant legislation, publishes bulletins and other literature and appears before organizations of physicians as well as professional and consumers groups, and it has been called upon to advise Congressional committees.

Among other activities the Physicians Forum has now taken up the fight for the passage of the Wagner-Murray-Dingell Bill (S 1050). The Forum has been asked by lay groups interested in this legislation to assume the leadership of those members in the medical profession who are interested in this important struggle.

Although the Physicians Forum has become national in scope, it is still rather limited in membership in certain areas. Its officers believe that there are many members of the medical profession belonging to their state societies who would welcome this method of expressing a minority (or perhaps majority) opinion. The Forum also believes that there are many members of the medical profession who favor this progressive program for the delivery of medical care to the great masses of American people proposed by the Wagner-Murray-Dingell Bill but are at sea in regard to how to register their feelings.

The Physicians Forum offers such an opportunity. Its membership at the present time is limited to members of county or state societies and the National Medical Association. Those physicians who are interested in joining the Physicians Forum, or who wish to learn more of its activities, may do so by applying to me or to the headquarters of the Physicians Forum at 510 Madison Avenue, New York City.

CHANNING FROTHINGHAM, M.D.

1153 Centre Street
Jamaica Plain 30, Massachusetts

COSMETICS CONTAINING HORMONES

To the Editor Your letter of July 6, 1945, asks what is the status of hormone-containing cosmetics so far as the Food and Drug Administration is concerned.

We have made some investigation of these products. There have been conflicting reports in the literature concerning the effects of estrogenic substances when applied locally. When applied in sufficiently large amounts there is no question but that they are absorbed and produce their usual systemic effects. When the amount of estrogens is reduced, however, to the quantity found in the products which are sold to laymen there seems to be no unanimity of opinion as to the physiologic effect. Some workers have reported the production of local edema apparently by imbibition of fluid into the collagen bundles without any systemic effect, others have claimed that it is not possible to produce a local result without at the same time causing a general one.

There has been a considerable amount of work on the car-

cinogetic properties of these materials. In highly susceptible strains of rats under very special conditions the administration of the estrogens has apparently produced carcinoma, but with ordinary laboratory animals and in all studies so far on human beings there is no evidence whatsoever that these products are carcinogenic.

We have investigated the files of a number of firms producing these products searching for evidence of injuries. We have not found such evidence.

To summarize, we have carefully reviewed the literature and consulted with many experts and, as a result of this, have arrived at the conclusion that at this time there is not sufficient legal evidence to show that the use of estrogens in the amounts found in products of this class is dangerous. We are skeptical of the benefits, if any, which accrue from the local use of these products but we do not believe that we are in a position to challenge qualified claims concerning them. We have consistently informed manufacturers that because of the uncertainty of the ultimate effect of the use of these products and because of their dubious value we do not look with favor on their distribution for lay use.

It was our plan to have conducted carefully controlled clinical studies to serve as the basis of appropriate legal action if the products proved to be worthless, but preoccupation of the medical profession with more important studies during the war and the fact that our own medical staff has been made very much smaller has not made it possible to conduct these studies. We hope that they can be made soon after the termination of hostilities.

P. B. DONNAN

Commissioner of Foods and Drugs

Food and Drug Administration
Federal Security Agency
Washington 25, D. C.

* * *

Although it is true that there is "no evidence whatsoever that these products are carcinogenic," the following statement (Nathanson, I. T. Endocrine aspects of cancer. *Am. Eng. J. Med.* 231 764-770 and 795-802, 1944) deserves serious consideration.

Strong evidence exists to indicate that endocrine factors are associated with some human tumors. There is as yet no conclusive proof that these influences are directly concerned with cancer, although an increasing number of cases are coming to light in which cancer developed after intensive estrogen therapy in organs such as the uterus and breast, which are normally stimulated by these hormones. It is probable that this is coincidence, but the association cannot be ignored. Present evidence suggests that the sex hormones are not in themselves carcinogenic. It is likely that, as a result of excessive stimulation or atypical metabolism, the tissues of susceptible persons are conditioned to the action of a carcinogenic agent. — Ed

ANTIBIOTICS

To the Editor The lack of good prefixes in Anglo-Saxon English has been one factor which has led to our pathetic and often laughable habit of making new words out of old Greek and Latin roots. The other factor is a natural instinct to hide our ignorance behind a false front of big words. Plain English words are always better than the jaw breakers that impressed our grandfathers.

Therefore a pox upon Dr. Wingo's "mycoantibiotics" and "chemoantibiotics" (a letter published in the July 19 issue of the *Journal*) and all other antibiotics. The silliness of the words is obvious when they are put into English mold against life, drug against life and so on. Why not mold germ killer or drug germ killer, if we must have novelty?

I also prefer high blood pressure to hypertension, cure or care to therapeutics, tired nerves to neurasthenia, grog shop or gin mill to liquor saloon, printing to typography, headache to cephalalgia and thousands of other plain, clear short words to their repulsive four, five or six jointed Greek and Latin equivalents. I wish more people felt the same way.

ROBERT W. BUCK, M.D.

5 Bay State Road
Boston 15

(Notices on page xiii)

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THE TREATMENT OF RHEUMATOID ARTHRITIS WITH 417 COURSES OF GOLD*

An Analysis of 259 Cases

ABRAHAM COHEN, M D,† JOEL GOLDMAN, M D,‡ AND ALFRED W DUBBS, M D §

PHILADELPHIA

MUCH has been written on the subject of gold as a therapeutic agent in the treatment of rheumatoid arthritis. Its merits are apparently undeniable, but its mode of action is still a matter of conjecture. There seems to be general agreement that gold is a dangerous drug and that extreme caution must be exercised in its administration. In this paper we wish to emphasize the matter of untoward reactions and the lack of influence of vitamin therapy on reactions as well as on treatment.

In 1943, two of us¹ reported the results of the treatment of 122 cases of rheumatoid arthritis receiving 176 courses of gold. In that report only 11 per cent untoward reactions were observed, his figure being based on the total number of courses given. Compared with the reports of other workers, this percentage was considered unusually low. The patients received, in conjunction with gold therapy, large amounts of orange juice and liver, and it was thought that one of these factors might have been responsible for the low incidence of untoward reactions.

On the basis of the above, treatment was begun with three new groups of cases. Gold was administered as in the previous study. Solganal-B Oleosum² was given intramuscularly in the following dosage: 10 mg twice weekly, 4 doses, 25 mg twice weekly, 4 doses, 50 mg twice weekly, 4 doses, and 100 mg weekly, 9 doses. This constituted a course. A rest period of at least six weeks was allowed between courses. One group received orally with the above 300 mg of ascorbic acid daily, and another group received 2 teaspoonfuls of vitamin B com-

plex three times daily. || Since most of the cases were ambulatory, it was deemed advisable to use Vitamin B complex orally in place of liver. This substance was more desirable since it permitted the elimination of another injectable preparation. A third group received gold without vitamins. Table 1 shows the number of cases treated by this method and the number of courses of gold received. We attempted by this method to determine whether one of the above factors might be considered a necessary adjunct to the treatment of rheumatoid arthritis, as well as an aid in the reduction of untoward reactions.

TABLE 1 Cases Listed according to Number of Courses and Type of Treatment

TYPE OF TREATMENT	NUMBER OF COURSES					TOTAL
	1	2	3	4	5	
Gold and vitamin C	65	35	11	6	1	118
Gold and vitamin B complex	29	16	11	8	2	66
Gold alone	43	7	5	2	2	57
Totals	137	58	25	16	5	241

As in the previous study,¹ patients were classified according to the grade of the disease and the improvement, as follows:

Class 1 Typical rheumatoid arthritis of less than one year's duration (subjective symptoms only)

Class 2 Changes in joints, with activity only slightly limited

Class 3 Changes in joints with greatly limited activity

Class 4 Dislocations, ankyloses and contractures (patient confined to bed or wheel chair)

Group 1 No improvement (NI)

Group 2 Improved (I)

Group 3 Much improved (MI)

Group 4 Very much improved (VMI)

*From the Arthritis Clinic, Jefferson Medical College Hospital and the Arthritis Clinic and Arthritis Wards, Philadelphia General Hospital.

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²Gold in the form of Solganal-B Oleosum was kindly supplied by Schering Corporation, Bloomfield, New Jersey, through the courtesy of Dr. Max Gilbert.

||The ascorbic acid and the vitamin B complex (Elixir Plebez) were kindly supplied by Wyeth Incorporated, Philadelphia. Two teaspoonfuls of the latter contains 40 mg. of niacin, 12 mg. of vitamin B (thiamine) and 0.5 mg. of vitamin B (riboflavin).

The 137 patients were graded according to the severity of the disease as follows. 4.4 per cent, class 1, 29.2 per cent, class 2, 65.7 per cent, class 3, and 0.7 per cent, class 4

Table 2 shows the results of treatment in a total of 118 courses of gold administered to 65 patients in the vitamin C and Solganal-B group. Table 3 shows the results obtained in treating 29 patients receiving 66 courses of gold, as well as vitamin B complex. It was observed that patients receiving vitamin B complex reported an improvement in

gold is begun, the patient is instructed to pay particular attention to itching, rash and sore mouth. In addition, he is told that any other symptom or sign that may arise should be noted, regardless of severity and regardless of what the patient may think the cause to be. These facts are reported at the next visit and if necessary, treatment with gold is discontinued until the symptom or symptoms disappear. Thus, if a patient reports slight itching for a few hours, treatment is stopped for one week. The appearance of conjunctivitis, simple

TABLE 2 Result of Treatment, according to Age, in Patients Receiving Gold and Vitamin C

THERAPEUTIC RESULT	AGES							TOTAL CASES	
	UNDER 20	20-29	30-39	40-49	50-59	60-69	70 AND OVER	NO	PERCENTAGE
Group 4 (VMI)	3	2	7	16	21	13	5	67	56.8
Group 3 (MI)	0	4	2	3	4	7	0	20	17.0
Group 2 (I)	0	2	3	5	5	2	0	17	14.4
Group 1 (NI)	0	2	0	1	6	3	1	13	11.0
Worse	0	0	1	0	0	0	0	1	0.8
Totals	3	10	13	25	36	25	6	118	

TABLE 3 Result of Treatment, according to Age, in Patients Receiving Gold and Vitamin B Complex

THERAPEUTIC RESULT	AGES							TOTAL CASES	
	UNDER 20	20-29	30-39	40-49	50-59	60-69	70 AND OVER	NO	PERCENTAGE
Group 4 (VMI)	3	4	4	8	13	4	0	36	54.5
Group 3 (MI)	0	2	5	3	1	2	0	13	19.7
Group 2 (I)	0	0	1	2	2	2	1	9	12.1
Group 1 (NI)	0	0	0	1	3	3	2	9	13.7
Worse	0	0	0	0	0	0	0	0	0.0
Totals	3	6	10	14	19	11	3	66	

TABLE 4 Result of Treatment, according to Age, in Patients Receiving Gold Alone

THERAPEUTIC RESULT	AGES							TOTAL CASES	
	UNDER 20	20-29	30-39	40-49	50-59	60-69	70 AND OVER	NO	PERCENTAGE
Group 4 (VMI)	0	0	10	6	8	8	1	33	57.9
Group 3 (MI)	0	0	0	1	7	6	0	14	24.6
Group 2 (I)	0	0	1	1	1	0	1	4	7.0
Group 1 (NI)	0	0	1	1	2	0	1	5	8.8
Worse	0	0	0	1	0	0	0	1	1.7
Totals	0	0	12	10	18	14	3	57	

appetite, and showed a more rapid gain in weight and a tendency toward less fatigue. The results obtained in the control group (patients who received no supportive measures), are shown in Table 4. Forty-three patients received 57 courses of treatment of Solganal-B alone.

As stated in the previous paper, we believed that patients presenting only subjective improvement should not be included among those having favorable results. Therefore, Table 5, summarizing the favorable results, includes only groups 3 and 4. According to these observations, the use of vitamins as an adjunct in the treatment of rheumatoid arthritis with gold is of little if any value.

As stated above, the previous report indicated a comparatively small percentage of untoward reactions. The steps taken to determine such reactions should be explained. When treatment with

dryness of the skin, severe headache, dizziness, pain in abdomen or diarrhea, is a good reason for interrupting treatment long enough to attempt to determine the cause.

The above symptoms, unless of reasonable severity, are not included in the category of untoward

TABLE 5 Summary of Favorable Results, according to Type of Treatment

Type of Treatment					
TYPE OF TREATMENT	GROUP 3		GROUP 4		GROUP 3 AND 4
	%		%		%
Gold and vitamin C	17	0	56	8	73
Gold and vitamin B complex	19	7	54	5	74
Gold alone	24	6	57	9	82

reactions. This may be one factor in the low incidence of what we consider to be untoward reaction. It is difficult to evaluate these simple symptoms but many are probably nothing more than wh

one would expect in a patient receiving no medication

Periodic blood counts and urinalyses were made. Again, we were unable to note any significant changes in the urine, except in 1 case. There were but 3 cases of severe anemia, all requiring transfusions, and when the red-cell counts were normal, treatment was resumed, one of these was fatal.

Table 6 lists the cases having symptoms severe enough to constitute untoward reactions. Eleven occurred during the first course, 8 during the second, 3 during the third, and 1 during the fourth. The incidence according to type of treatment was as follows: vitamin C and gold, 13.6 per cent (16 in 118 courses), vitamin B complex and gold, 6.1 per cent (4 in 66 courses), and gold alone, 5.3 per cent

and the sedimentation rate 145 mm (Westergren). The patient was admitted to Jefferson Hospital, where she was transfused four times with 500 cc. of whole blood at each transfusion. She was discharged after 2 weeks. At the time of discharge there was little improvement in the condition of the joints, but examination of the blood showed the following: hemoglobin 71 per cent, red-cell count 4,200,000, white-cell count 7,500, and sedimentation rate 145 mm.

The patient suffered considerably from the arthritis, getting little relief from analgesics. She received 10 mg of Solganal-B Oleosum twice weekly for four doses, 25 mg twice weekly for four doses, and 50 mg twice weekly for four doses. With each dose she received 4 units of crude liver extract. At the end of this 6-week period, she developed a stomatitis, but during treatment the improvement in the joints was dramatic. The pain and swelling completely subsided. There remained only slight stiffness, which was particularly manifest in the early hours of the morning before rising. It was originally intended that the patient should receive a full course of gold, but since a stomatitis developed, gold was stopped and crude liver extract in doses of 4 units three times weekly intramuscularly was substituted.

TABLE 6 Untoward Reactions in 137 Patients (241 Courses)

VITAMIN C AND GOLD	DOSE OF GOLD mg	VITAMIN B COMPLEX AND GOLD	DOSE OF GOLD mg	GOLD ALONE	DOSE OF GOLD mg
Course 1 (11 reactions)					
Pruritus	740	Pigmentation of lips	640	Exfoliative dermatitis	240
Pruritus	840	Pruritus	540	Anemia	640
Seborrhea	150	Seborrheic dermatitis	640		
Pruritus with papular eruption	240				
Pruritus	540				
Pruritus	940				
Course 2 (8 reactions)					
Pruritus	840				
Seborrheic dermatitis	240				
Pruritus	940				
Albuminuria	440				
Seborrheic dermatitis	640				
Purpura hemorrhagica (patient died)	990				
Bronchitis	340				
Papular dermatitis	540				
Course 3 (3 reactions)					
Seborrheic dermatitis	440			Gold bronchitis	440
Anemia	540				
Course 4 (1 reaction)		Cholecystitis with hepatitis	1040		

(3 in 57 courses). The over-all incidence was 9.5 per cent (23 in 241 courses). It is obvious that neither vitamin B complex nor vitamin C in fairly large doses influenced the number of untoward reactions encountered in the treatment of rheumatoid arthritis with gold.

To emphasize the importance of caution the following case, the only fatality in the series, is given in some detail.

A B, an 18-year-old girl, was first seen on June 19, 1943 with a chief complaint of stiffness, soreness and swelling in all the joints of the upper and lower extremities. Three months previously, she had noticed on arising that her hands were stiff. She paid little attention to this, but in a few days there was swelling. Soon the elbows and shoulders were stiff and sore and it became increasingly difficult to do her work as a clerk. Two weeks after the onset of the illness, she was confined to her home. At that time there was also severe pain and swelling in the ankles and knees. The condition was progressing slowly when she was seen by one of us.

Physical examination at that time showed that the joints of the fingers, wrists, elbows, shoulders, knees, ankles, toes and cervical vertebrae were involved. There was typical uniform swelling of the fingers and considerable limitation of motion in most of the joints. The hemoglobin was 41 per cent, the red-cell count 2,700,000, the white-cell count 11,700,

After 2 weeks of treatment with liver extract only, the stomatitis began to improve, however, there was an exacerbation of the joint difficulty. The hemoglobin was 78 per cent, the red-cell count 5,800,000, the white-cell count 7,800 and the platelet count 240,000. During the following 2 weeks the arthritis was as severe as before treatment.

At the end of the 6th week, the stomatitis had disappeared but the arthritis was worse than ever before. The patient and her mother, insisting on resumption of gold therapy, were fully apprised of the serious dangers attendant on such a course. They assumed full responsibility for all eventualities and treatment was resumed with lower dosages. Twenty-five milligrams was administered at weekly intervals from October 18, to April 1, 1944. Four weeks after the new course of treatment was started improvement in the joints was again noted. The improvement continued until March 25 when the patient began to have slight pain in the joints. At that time the hemoglobin was 72 per cent, the red-cell count 3,550,000, the white-cell count 6,200, and the platelet count 260,000. Because of the slight exacerbation of pain it was decided to increase the dose of gold to 50 mg. Up to that point gold had been well tolerated. The following week, the patient presented bleeding from the gums and purpuric spots over the feet and legs. She was admitted to the Philadelphia General Hospital on April 3, with the diagnosis of rheumatoid arthritis and thrombocytopenic purpura due to gold therapy.

While in the hospital she received fifteen 500-cc transfusions of whole blood, but the red-cell count never rose above

In respect to sedimentation rates, the previous paper¹ showed that they returned to normal in only 7.3 per cent of the cases. The whole group of 259 cases shows that in 8.1 per cent of those receiving 1 course of gold, 7.3 per cent of those receiving 2 courses and 14.3 per cent of those receiving 3 courses, the sedimentation rates returned to normal. In those cases that did not return to normal after 3 courses, the sedimentation rate remained rapid even after 4 or 5 courses.

Gold is not usually administered to patients who have a normal sedimentation rate, occasionally, however, one encounters a case that responds to no other treatment, and in desperation one uses gold. Such has been the case with 9 of our patients. Of these, 4 showed excellent results and 2 were decidedly improved. One was unimproved, and 2 showed only subjective improvement. It appears, therefore, that withholding this drug from patients because the sedimentation rate is normal is not always justified. One should not hasten to use gold, however, when the sedimentation rate is normal. It should be employed only as a last resort. There were no untoward reactions in this group.

The sedimentation rates were reduced in 72.9 per cent of cases given the first course of treatment. In 35.5 per cent the rate was reduced only moderately, whereas in 37.4 per cent it was reduced by 50 per cent or more.

Thirty-three cases (12.7 per cent) showed an increase in the sedimentation rate following a single course of treatment. Fourteen were very much improved, and 5 were much improved. Thus, 19 patients showed both subjective and objective improvement in spite of an increase in sedimentation rate. Thirty-five patients showed an increase in sedimentation rate following 2 courses. Of these, 21 were both subjectively and objectively improved. Eleven cases likewise showed an increase in sedimentation rate following 3 courses, 6 patients being improved. In 7 cases the rate was increased after 4 courses, and 6 patients showed similar improvement. Although it is true that the reduction in sedimentation rate indicates favorable progress, it is also true that an increasing sedimentation rate does not always mean unfavorable progression of the disease.

It is curious that there is obvious objective improvement and apparent freedom from discomfort in these cases, yet the sedimentation rate remains rapid. We are continuing to keep a goodly number of these patients under observation to determine whether the improvement is temporary and whether the sedimentation rate is as important as we think it to be at present.

The arthritis clinics at Jefferson Medical College and Philadelphia General hospitals have been active fifteen and nineteen years, respectively. In prospect, it is with a great deal of satisfaction that we are able to make this report. For years we have stood by and observed our patients progress

from an early rheumatoid arthritis to permanent invalidism. We have removed foci of infection and have used vaccines and bacterial filtrates, both subcutaneously and intravenously, sulfur, chemicals, analgesics, physiotherapy, bee venom, snake venom, vitamins and so forth. Occasionally the effects obtained appeared encouraging, however, after continuation of one form of therapy or another a stalemate was reached. Gold therapy, on the other hand, has given us a new hope for these sufferers. We have been working with gold compounds for about five years, and consider that of all the drugs used, none have been so promising. It is true that we are not in a position to call our patients cured. There are many, however, in whom the condition has remained apparently arrested for a few years.

We are attempting to follow our cases and hope soon to report on the progress made by them. This is difficult, especially when dealing with ambulatory cases. It may be that some day more may be learned about the etiology of rheumatoid arthritis and that a specific remedy may be found. Until that day arrives, it is our opinion that gold therapy judiciously used offers the best therapeutic approach.

SUMMARY

Two hundred and fifty-nine patients with rheumatoid arthritis have been treated with from 1 to 5 courses of gold in the form of Solganal-B Oleosum, for a total of 417 courses.

The giving of 300 mg. ascorbic acid daily did not aid in the reduction of untoward reactions in 65 patients receiving 118 courses of gold.

Vitamin B complex was not a factor in reducing untoward reactions in 29 patients receiving 66 courses.

The percentage of improvement was no greater in the groups receiving vitamins as an adjunct than it was in the group of 43 patients receiving 57 courses of gold alone.

One fatality due to thrombocytopenia purpura is reported in detail. Because of objective improvement in 88 per cent of the various courses of treatment, gold preparations are recommended for the treatment of rheumatoid arthritis, but extreme caution must be exercised.

A normal sedimentation rate is not always a contraindication to gold therapy.

An increasing sedimentation rate during treatment is not always an indication that clinical improvement is not to be expected.

There were untoward reactions in 10.3 per cent of 417 courses of treatment, however, there were untoward reactions in only 8.9 per cent of 259 patients receiving a single course of gold. In the 96 patients receiving 2 courses of gold, the percentage of untoward reactions rose to 15.6 per cent.

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ACTIVE IMMUNIZATION AGAINST SCARLET FEVER*

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THERE are a substantial number of physicians who are opposed to active immunization against scarlet fever, claiming that the accompanying reactions are unusually severe. The presence of this opposition, despite the fact that such immunization has been shown to be effective,¹⁻³ is thought provoking, and for this reason, a report is presented of the reactions in 377 private patients actively immunized against scarlet fever during the last thirteen years.

The purpose of this paper is to describe a method of active immunization against scarlet fever through use of graduated doses of scarlet-fever streptococcus toxin that was found effective both in completely immunizing against scarlet fever and in minimizing the frequency and severity of the reactions and to furnish an analysis of the resultant reactions in 340 children.

PROCEDURE

Nine patients were immunized in 1933 according to the method suggested by Dick.⁴ Five weekly injections of 250 units, 2000 units, 8000 units, 25,000 and 80,000 units, respectively, were given to each child. The series of injections was preceded and followed by a Dick test. Because of the frequency — 21 of the 45 injections were followed by a general reaction — and severity of the reactions, however, and because 4 of the patients had positive Dick tests at the end of the series, an attempt was made to increase more gradually the number of units of toxin given before reaching the final dose.

Twenty-eight patients were divided into three groups during 1933 and 1934 and immunized by means of six, seven and eight injections, respectively, given at one-week, two-week and three-week intervals. It was soon determined that the most effective method with the lowest incidence of general reactions, was that of seven consecutive weekly injections, and that method was employed in immunizing 340 children in subsequent years.

The injections were given subcutaneously in the following doses: 650 units, 2500 units, 5000 units, 10,000 units, 25,000 units, 55,000 units and 110,000 units, a total of 208,150 units. If a moderate or severe general reaction occurred, the same dose was repeated the following week. In case of an allergic reaction, the injections were stopped. Immunization was conducted during the spring or fall, preference being given to the late spring. This

was done because respiratory infections are less frequent then than at other times, which obviated the tendency of parents to blame the injections for all the infections and ailments that might develop independent of immunization.

The patient was permitted his usual regime. Recent upper respiratory infections and a history of allergic sensitivity in the patient or in the family were noted. The mother was instructed to note the reactions, both local and general. Local reactions were considered those that involved redness and tenderness at the site of the injection, general reactions included nausea and vomiting, fever, rash, itching, malaise, marked fatigue, irritability, muscular stiffness, nasal hemorrhages, pallor, cold sweats and headaches — alone or in any combination.

Immunization was confined to children over one year of age. The Dick test was given before and after the series of injections during 1935 to 1944, inclusive. If the subsequent test was positive, another series of injections was immediately begun. In the group of 72 children immunized during 1945, the Dick test was not done in the pre-school group and it was used only to test for immunity before the series of injections were given in the others.

The reactions following the seven weekly injections were carefully studied. Since local reactions rarely caused concern to the parents, only the general reactions were analyzed with reference to frequency, type, age and a history of allergic sensitivity in the patient or the family.

A special study was made of 27 children who were immunized against scarlet fever during April and May, 1939, and of 71 patients similarly immunized during the same period in 1944. All these children were immunized just after an epidemic of upper respiratory infection due to a hemolytic streptococcus had occurred in the community. A study was also made of 10 children who had been in direct contact with a case of scarlet fever just previous to immunization.

RESULTS

The general reactions were comparatively infrequent (Table 1). Of 2357 injections given, only 166 (7 per cent) produced general reactions. The most frequent of these was nausea and vomiting, rarely accompanied by diarrhea or abdominal pain, it occurred 91 times (Table 2). The children were pale, perspired freely and vomited, usually from one to three times, although some patients vomited as many as nine times. Most of these reactions

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occurred two or three hours after immunization. An elevated temperature was present 40 times, a rash 12, and fatigue 7. Four children had allergic reactions, and muscle pains were noted 4 times.

TABLE 1 *Relation of General Reactions to Injections*

INJECTION	DOSE UNITS	NO OF INJECTIONS	GENERAL REACTIONS NO	PERCENTAGE
First	650	340	21	6.2
Second	2,500	339	36	10.6
Third	5,000	336	33	9.8
Fourth	10,000	336	26	7.7
Fifth	25,000	335	16	4.8
Sixth	55,000	334	18	5.4
Seventh	110,000	334	16	4.8
Eighth (repeat)		3	0	0.0
Totals		2357	166	
General average				7.0

One child developed nasal bleeding thirty-six hours after 4 of 8 injections. Itching of the skin occurred in 2 children, headache resulted in 1, and swelling

TABLE 2 *Type of General Reaction Following Immunization*

TYPE OF REACTION	NO OF REACTIONS	PERCENTAGE OF TOTAL
Nausea and vomiting	91	54.8
Elevation of temperature	40	24.1
Rash	12	7.2
Fatigue	7	4.2
Muscle pain or lameness	4	2.4
Nasal bleeding	4	2.4
Allergic reaction	4	2.4
Itching of skin	2	1.2
Headache	1	0.6
Swelling of axillary lymph nodes	1	0.6

of the axillary lymph nodes in 1. In 28 children there was more than one reaction.

Total immunity to the scarlatinal toxin of the hemolytic streptococcus was apparently afforded in practically every case. After completing the series of injections, only 3 of the entire series of 268 patients immunized prior to 1945 had a positive Dick test, thus requiring a second series of injections. Furthermore, no case of scarlet fever has developed among these children.

The percentage of general reactions during immunization was lowest (4.7) in the youngest patients, those between the ages of one and two (Table 3). The highest rate (17.0 per cent) occurred in those

TABLE 3 *Relation of General Reactions to Age*

AGE	NO OF CHILDREN	NO OF INJECTIONS	GENERAL REACTIONS NO	PERCENTAGE
1	181	1267	59	4.7
2	36	394	35	8.9
3	35	245	29	11.4
4	15	105	9	8.6
5	15	103	8	7.8
6	13	88	15	17.0
7 to 11	25	155	11	7.1
Totals	340	2357	166	

between six and seven years old, and the next highest (11.4 per cent) in those between three and four. The rates in the other age groups ranged from 7.1 to 8.9 per cent.

In April and May of 1939 and 1944 there was present in the vicinity of Boston a mild epidemic

of upper respiratory infection due to different strains of hemolytic streptococcus. Fifteen of the 98 patients immunized at these times had a general reaction following the first injection.

Of the 10 children who had been in close contact with a scarlet-fever patient just previous to immunization, 2 had general reactions after the first injection, 5 had unusually marked local reactions, consisting of redness and swelling of the upper arm about the site of the injection, and 3 had no unusual general or local reaction.

There were 140 children who had a family or personal history of allergic sensitivity. Of these only 4 developed allergic reactions during immunization. The reactions consisted of swelling of the face, including the eyelids, nose and lips, and of the tongue, dyspnea and a maculopapular rash (2 children). In 1 child the reaction followed the first injection, and in 3 it followed the second.

DISCUSSION

The peak of positive Dick reactions in children is between the ages of one and two years, being over 90 per cent, and the incidence of general reactions during scarlet-fever immunization is lower at this age level than at any other. Because of the high percentage of positive Dick reactions in pre-school children, Bacon⁵ suggests that all children of this age be assumed to be susceptible to scarlet fever and that active immunization follow as a matter of routine, as is customary in diphtheria immunization. This suggestion was followed in the 72 children in this series immunized in 1945.

There was an interesting similarity between the percentage of general reactions in the 98 children immunized during the epidemics of 1939 and 1944 and that in the 10 children actively immunized after having been in direct contact with scarlet-fever patients. In the first series the percentage was 15, whereas in the second series it was 20. The similarity would be even more striking, 18 as compared with 20 per cent, if 3 children not included among the former are added. These children, aged one, two and four years, respectively, were given the first injection following a recent upper respiratory infection, one of them in 1939 and the other two in 1944. They developed a local reaction, with rectal temperatures of 101 to 103° F. The parents refused further immunization. In these 108 children there were seventeen general reactions following the first injection, as compared with only four general reactions following the corresponding injection in the remaining 232 children.

These reactions were not due to the presence of a nonspecific upper respiratory infection for in the spring of 1945 there was a widespread upper respiratory infection in the community. Of 72 children immunized, 31 had upper respiratory infections, however, only three general reactions followed the first immunizing dose. This suggests

that when hemolytic streptococcus infection is present in the community, a higher proportion of persons than usual are sensitive to the initial immunizing dose of scarlet-fever toxin. The work of Lancefield⁶ and Griffith,⁷ who by a precipitation reaction and an agglutination technic proved the existence of many different serologic types of streptococci associated with human infection, is pertinent in this respect. All these types may be associated with typical scarlet fever, some much more frequently than others. These same types have also been isolated from cases of septic sore throat, tonsillitis, erysipelas, otitis media and other nonscarlatinal infections.

None of the 10 children immunized after exposure to scarlet fever developed the disease. Although this suggests that the immunity response in susceptible children when given a single dose of scarlet-fever toxin after contact with the disease is rapid enough to prevent infection, such a thing seems unlikely in view of the short incubation time of the disease and the appreciable time usually required for the development of immunity.

A history of allergic sensitivity does not preclude immunization against scarlet fever in children, as shown by the fact that only 4 of the 140 patients with such a history developed an allergic reaction. Apparently the procedure of choice is to immunize routinely irrespective of sensitivity, but to stop the immunization if an allergic reaction occurs following an injection.

The reactions described in this paper may have been due either to the direct toxic action of the immunizing agent or to hypersensitiveness to some constituent of it — perhaps a nucleoprotein.

Although it was impossible to gather adequate comparative statistics, the impression was gained that the nonscarlatinal hemolytic streptococcus infections that occurred among the immunized patients were less both in frequency and in severity than they would have been without immunization.

SUMMARY AND CONCLUSION

A modified method for active immunization against scarlet fever is described. Seven weekly injections are given, which result in fewer general reactions and a higher degree of immunity than are obtained following the usual Dick method.

The incidence of general reactions was 7 per cent among 340 children between one and twelve years of age immunized during the last eleven years. The most frequent general reaction was nausea and vomiting.

Ten scarlet-fever contacts and 98 children actively immunized during epidemics of upper respiratory streptococcal infections had high incidences of general reactions — 20 and 15 per cent, respectively — following the first immunizing dose.

Immunity, as evidenced by a negative Dick test, was complete in 98.9 per cent of the children, a repeat injection being given to the others. With such a high percentage of immunity, a follow-up Dick test is probably unnecessary.

None of the 340 patients developed scarlet fever.

The best age to immunize actively for scarlet fever is between one and two years. The incidence of general reactions was lowest in this group. Since there is a scarlet-fever susceptibility of over 90 per cent at this age, an initial Dick test is not necessary.

A history of allergic sensitivity is not a contraindication to immunization.

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CLINICAL NOTE

SPONTANEOUS RUPTURE OF A
NORMAL SPLEEN

REPORT OF A CASE

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ALTHOUGH it is difficult to accept the idea that the normal spleen can rupture under normal physiologic conditions, a relatively small number of cases of seemingly proved authenticity have been reported in the surgical literature during the last twenty years.

There are various theories adopted to substantiate spontaneous rupture of the spleen. Susman¹ has summed up the process of spontaneous rupture as follows: softening of all structures of the spleen, congestion of the portal vein and its radicles and inability of the narrower splenic vein to accommodate itself, blood thus being forced between the spleen and investing peritoneum, which finally gives way, and perisplenic adhesions which by fixing the organ predisposes to rupture. Byford² in reporting a case stated his belief that the spleen was not normal in its entirety and that the rupture occurred at a localized diseased area, which was destroyed by the hemorrhage resulting from the rupture. Rhame³ believed that the engorgement of the spleen with blood during digestion might predispose to rupture. Zuckerman and Jacob⁴ reported 20 cases of spontaneous splenic rupture. Many reported cases show disease of the gastrointestinal tract, especially of the gall bladder. Roettig et al.⁵ hold that these cases represent instances of delayed rupture, the history of trauma being overlooked, and that there may be latent periods as long as six months before rupture occurs in a previously traumatized spleen.

Spontaneous rupture of the pathologic spleen is not infrequent and has been reported from in cases of typhoid fever, leukemia, malaria, hemophilia and pregnancy. Such a case during the last trimester of pregnancy was reported to me shortly after the following case occurred:

S C (J H 30095) a 28-year-old married woman, entered the Jordan Hospital on March 9, 1944. The night before admission she was awakened by sharp pains in the upper abdomen, which interfered with breathing. The pains were not localized. She had to sit up to catch her breath, and on doing so felt cold and sweaty. Soon after this she fainted while moving her bowels, this apparently resulted in no injury. After being revived she breathed more easily but she could not move on account of the persistent upper abdominal pain. A few hours after the onset of the pain she noted pain in both shoulders. There was no nausea or vomiting. The bowels were regular. There were no urinary or other gastro-

intestinal symptoms. The regular menstrual period began on this day, without dysmenorrhea.

The past history was essentially negative. A normal delivery had occurred about 2 years previously.

Physical examination showed a well developed and well nourished woman, with a pallid skin and complaining of abdominal pain. The temperature was 100.6°F. The examination was otherwise negative except for the abdomen, which was doughy and spastic throughout, especially in the left upper quadrant. There was diffuse pelvic tenderness on vaginal examination. No masses were palpable. The consulting gynecologist, Dr M O Belson, thought that there was active intraperitoneal bleeding, probably secondary to ectopic pregnancy.

The patient was given 1 unit of plasma and prepared for laparotomy. Under ether anesthesia a low midline incision was made. There was considerable free blood in the lower abdomen and pelvis. Careful survey of the uterus, tubes and ovaries was negative. There was no bleeding from the broad ligaments. There was an ecchymotic area subperitoneally near the uterine end of the left sacrouterine ligament. This was opened and inspected, but no active bleeding was noted. It was apparent that the pelvis and pelvic organs were not responsible for the bleeding. The cecum and lower ileum and the liver were normal. On palpating the spleen it was obvious that the source of bleeding was coming from a rent in the convex surface near the upper pole.

By that time the patient was in a critical condition from loss of blood, the exploratory palpation having aggravated the bleeding. The lower incision was extended upward to the left costal margin, all clots were removed, and a splenectomy was rapidly performed, only the splenic pedicle requiring ligature. The lower incision was closed in layers, the upper incision was closed with single through-and-through cotton sutures. A rubber drain was placed in the left gutter near the splenic bed. Owing to the pulpy softness of the spleen and the haste necessary to complete the operation on account of the patient's condition the spleen was traumatized during removal.

At the close of the operation the patient was moribund, cold and pulseless, the blood pressure was not obtainable. A vein was exposed in the antecubital fossa and 1500 cc of citrated blood and 2 units of plasma were given, with good improvement.

The postoperative course was fairly uneventful. The temperature rose to 103°F the day following operation and fluctuated up to 101°F for 1 week, after which it remained normal. The wounds healed without infection. The patient received intravenous sulfadiazine, vitamin K, ferrous sulfate and liver extract during convalescence. The blood picture before discharge showed a mild secondary anemia.

The spleen was examined in the Lears Laboratory, with the following report:

The specimen consists of a spleen weighing 340 gm and measuring 15 by 10 by 4 cm. On the diaphragmatic lumbar surface there are multiple lacerations, two of the largest being situated one on either pole. The latter are jagged and measure roughly 6 cm in length. They appear to lift up the flaps of tissue. There is a small linear superficial longitudinal tear 6 cm in length in the midportion of this surface, and a deep incised laceration along one of the lateral borders extending inward 4 cm. The hilar surface presents many irregularities, with an excavation 5 by 4 by 1 cm. It is probable that this excavation represents the effects of operative trauma, and the incised and longitudinal lacerations may be similar defects. From their appearance the polar lacerations on the diaphragmatic and lumbar surfaces may well have been the result of pre-operative trauma.

On section the capsule is extremely thin, and the cortex is nodular, red-brown and extremely pulpy, with indistinct follicles and trabeculae. Microscopically the section demonstrates the usual splenic architecture, with well formed follicles and distinct sinusoids and trabeculae. There is evidence of hemorrhage in the traumatized areas.

Diagnosis: ruptured spleen.

*It is appreciated that the spleen weighed nearly twice as much as the generally accepted limit of normal. On the other hand, the reason for the increase in weight was not evident from microscopic examination nor has the patient subsequently developed a condition such as leukemia that might have accounted for the splenic enlargement.

*Surgeon Jordan Hospital, Plymouth, Massachusetts

SUMMARY

A case of rupture of the spleen is reported in which there had been no history of trauma, either recent or remote, in a previously well woman

I am indebted to Dr F J Abate for the opportunity to report this case

345 Court Street

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MEDICAL PROGRESS

PRACTICAL ASPECTS OF OXALATE METABOLISM*

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THERE are a wide variety of substances involved in human nutrition. The extensive literature dealing with the more important ones — vitamins, proteins, iron, glucose and so forth — tends to overshadow the modest literature concerning a wide range of less known and often less important substances of nutritional significance. As a result, many physicians fail to give them even a limited attention they deserve. Therefore, it is well periodically to re-emphasize subjects that are in general poorly understood.

Many common foods contain organic acids. Citric, malic, oxalic, tartaric, benzoic, lactic, isocitric, malonic, succinic, aconitic, tricarballic, salicylic, quinic and glyoxylic acids are representative organic acids found in foods. These vary widely not only in the amount and frequency of occurrence in various foods but likewise in their nutritional and metabolic significance for human beings. The papers by Smith and Orten¹ and by Mattice² may be consulted for a general discussion of this subject. Smith and Orten concisely state the problem in these words:

The presence of a number of the organic acids in mammalian tissues and body fluids has been repeatedly demonstrated. Questions therefore arise regarding the origin, possible effects and ultimate fate of these substances in the organism. Obviously, they may be derived from the preformed acids in ingested food. However, there is convincing evidence that certain acids are endogenous in origin and that they may be formed in the course of the metabolism of the carbohydrates, fats or proteins. Also, there are increasing indications that certain organic acids are not fortuitous constituents of living matter but that they are involved in definite physiological processes.

It is the purpose of this report to discuss one of these, namely, oxalic acid, which is a dicarboxylic acid with the formula $\text{HOOC}=\text{COOH}\cdot 2\text{H}_2\text{O}$. There is a considerable but widely scattered literature,

chiefly in German, French, Italian and English. Our interest in this acid was stimulated several years ago while studying a forty-three-year-old woman who had repeated attacks of oxaluria with renal colic and hematuria, with persistence of this syndrome in spite of the use of a low-oxalate diet.

OXALIC ACID CONTENT OF FOOD AND ITS RELATION TO THE AVAILABILITY OF CALCIUM

Oxalic acid is present in many foods. This represents the exogenous source of part of the blood and urine oxalates normally present in man. Table I gives data on the oxalic acid content for some representative foodstuffs, compiled from different sources.³⁻⁷ For more detailed information and for values for other foods these original sources can be consulted. The analyses by Kohman⁷ are the most modern and extensive. These reported values are of help to the physician in enabling him to prescribe a diet low in oxalic acid if it appears indicated for therapeutic purposes.

It is apparent that oxalic acid is widely distributed among the common foodstuffs. Chocolate, cocoa, tea and certain vegetables contain relatively large amounts, whereas fruits, meats and certain other foods contain little or frequently none. Of the vegetables, on the basis of Kohman's determinations, spinach, Swiss chard, New Zealand spinach, beet tops, lamb's quarters, poke, purslane and rhubarb have high contents. In contrast, peas, cucumbers, radishes, cauliflower, squash and turnip contain no oxalic acid. Most vegetables range between these two extremes.

Because the leafy vegetables serve as a valuable source of dietary calcium, much interest has been shown in the study of the effect of oxalates on the availability of calcium. In view of the prominence given by nutritionists as well as by comic-strip artists to the ingestion of spinach, it is not surprising that much of the research has been centered around this vegetable.

Most reports⁸⁻¹⁵ agree that the oxalic acid content of spinach (*Spinacea oleracea*) and New Zealand

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pinach (*Tetragonia expansa*) is high, often 10 per cent of the dried substance. The oxalate is present primarily in the form of insoluble calcium oxalate

make unavailable its own calcium but also to precipitate an equal amount of calcium supplied by other foods in the diet

TABLE 1 Oxalate Content of Common Foodstuffs (Expressed as Percentage of Oxalic Acid)

Food	ESBACH ² %	ARBENZ ⁴ %	WIDMARK ⁵ %	MAJUMDAR AND DE ⁶ %	KOHMAN ⁷ %
Vegetables					
Beets (leaves)	—	—	—	—	0.916
Spinach	0.191–0.327	0.29	0.837	0.658	0.892
Spinach New Zealand	—	—	—	—	0.890
Swiss chard	—	—	—	—	0.645
Rhubarb (stalks)	0.247	0.32	0.396–0.511	1.356	0.500
Sorrel	0.274–0.363	0.27	1.772–2.265	—	—
Beets	—	0.03	—	0.0404	0.138
Potatoes sweet	—	—	—	—	0.056
Beans wax	0.0312	0.045	0.039	—	0.041
Celery (stalks)	0.0025	Trace	—	—	0.034
Carrots	0.0027	—	0.016	0.0056	0.057
Endive	0.0045	0.005	—	—	0.0275
Onions	0	0.005	0.055	0.001	0.025
Turnips (leaves)	—	—	—	—	0.0146
Kale	—	—	—	—	0.015
Escarole	0.0017	—	—	—	0.0116
Peas	0	—	0.056	0.006	0
Beans lima	0.0158	—	—	—	0.0045
Asparagus	0	0.009	0	—	0.0052
Broccoli	0	—	—	—	0.0054
Cabbage	0	—	0.010	0.0059–0.0185	0.0077
Brussels sprouts	0.002	0.004	—	—	—
Corn	Trace	—	—	—	0.0014
Lettuce	0	—	0	0.0156	0.0071
Potatoes white	0.0046	0.04	0	0.015	0.0057
Squash	—	—	0.007	—	0
Cauliflower	—	0.006	0	0.0068	0
Cucumbers	0	—	0	—	0
Fruits					
Gooseberries	—	—	0.027	—	0.058
Raspberries, black	0.0062	0.05	—	—	0.055
Grapes	0	—	—	—	0.025
Oranges	0.005	0.01	0.028	—	0.024
Currants	0.013	0.05	0.066–0.072	—	0.019
Strawberries	0.0012	—	0.020	—	0.019
Blackberries	—	—	—	—	0.018
Blueberries	—	—	0.044	—	0.015
Raspberries red	0.0062	—	0.042	—	0.015
Apricots	Trace	—	—	—	0.014
Plums	0.007	Trace	0	—	0.010
Prunes	0.012	—	—	—	0.0058
Bananas	—	—	—	—	0.0064
Peaches	Trace	Trace	—	—	0.0050
Pears	0	0.02	0	—	0.0030
Pineapples	—	—	—	0.0058	0.0065
Tomatoes	0.0002–0.0072	0.008	0	0.0036	0.0075
Apples	Trace	Trace	0	—	0
Grapefruit	—	—	—	0.0034	0
Lemons (juice)	0.003	Trace	0.055	—	0
Melons	0	0.003	—	—	0
Miscellaneous					
Tea black (dry)	0.375	1.45	1.386	0.2192	—
Cocoa	0.352	0.48	0.645	0.442	—
Chocolate	0.09	—	—	—	—
Coffee	—	0.08	0.043	0.0154	—
Wheat flour	0	Trace	0	0.0111	—
Rye flour	0	—	0	—	—
Corn meal	—	0	—	0.0099	—
Rice	0	0	—	0.0046	—
Bread white	0.0047	—	—	—	—
Beef	—	—	0.025	—	—
Milk	—	—	0.0019	—	—
Mutton	—	—	0.0059	—	—

ystals, which can be demonstrated in microscopic sections of the leaves. The calcium content also is high. It has been estimated,¹⁴ however, that the oxalate content of spinach is sufficient not only to

Experiments on rats have shown that the calcium in pure calcium oxalate supplied orally is not utilizable.¹⁵ Soluble oxalates added to the diet interfere with the utilization of calcium carbonate¹⁶ or of

calcium supplied in skim milk^{17, 18} as a result of the formation of the insoluble calcium salt. Numerous investigators^{7, 10, 11, 14-17} have demonstrated that when spinach provides the calcium content of the diet to varying degrees, calcium retention is markedly less than in similar experiments in which the source is skim milk or one of the vegetables with low oxalate content. Growth is depressed,^{7, 14} the animals appear weak and unkempt,¹¹ mortality is increased,⁷ bone and tooth development is impaired,⁷ and reproduction is unsuccessful.⁷ MacKenzie and McCollum,¹⁹ on the other hand, demonstrated that in the rat if potassium oxalate is added to an adequate diet no deleterious effects result unless the oxalate concentration is 2.5 per cent or a simultaneous deficiency of vitamin D, calcium or phosphorus occurs.

Nutritional studies on man have not been so numerous. Interest in the literature has centered chiefly in the oxalic acid content of foods and its possible adverse influence on calcium metabolism. Edelstein et al.¹² report that the calcium of spinach is poorly utilized by young infants. Bonner et al.²⁰ in a well controlled experiment showed that the addition of 100 gm. of puréed spinach or its equivalent in oxalic acid to the daily dietary of 10 growing children caused no significant variations in the nitrogen, calcium or phosphorus utilization. No toxic effects were noted during the period of the experiment. Similar findings have been reported in adults.¹³

It seems, therefore, that under conditions of certain animal experiments the calcium of spinach is nonavailable for bodily utilization and that this is related, at least in part, to the oxalic acid content of the spinach.

The Council on Foods of the American Medical Association¹³ in a detailed report on the nutritional value of spinach, summarizes its conclusions on this point as follows:

Metabolism experiments show that the feeding of spinach is of no value during early infancy as a source of calcium, there is of course, plenty of calcium in milk to meet the needs of normal infants. The evidence also shows that in young children and in adults receiving diets adequate in calcium content the inclusion of spinach does not adversely affect the calcium metabolism.

This is therefore a reasonable and practical view for the physician to take.

TOXICOLOGY

Oxalic acid is an example of a toxic substance that is consumed with impunity in small amounts in the daily food, yet when ingested in large amounts in pure form causes serious illness or death. It has considerable toxicologic interest. Knowledge of the oxalates is said²¹ to date from the middle of the seventeenth century, at which time Duclos mentioned that "salt of sorrel," or potassium oxalate, could be obtained from the plant *Oxalis acetosella*.

In 1773, Savary obtained oxalic acid from the potassium salt. In 1776, Bergmann obtained "acid of sugar" by oxidation of glucose with strong nitric acid, and this was subsequently shown by Scheele to be identical with the acid obtained from the plant *oxalis*. Oxalic acid has had various household and industrial uses, such as bleaching of cloth and straw, dyeing and calico printing, cleaning of leather and woodwork, scouring of brass and copper and removing of ink stains. It can be readily purchased in a drugstore and is widely used in industry. Druggists are required to keep a record of sales.

An acute illness or even fatal poisoning^{21 2-3} may follow the ingestion of oxalic acid or one of the soluble oxalates. Because of their extremely sour taste these substances are seldom used in cases of homicide, but they may be ingested accidentally or with suicidal intent. Their close superficial resemblance to Epsom salts has been responsible for many cases of accidental poisoning, and their availability as household bleaching and cleaning agents has made them occasional mediums for attempted suicide.

Acute poisoning is much more frequent than is chronic. Only a few cases of the latter have been reported, and it is therefore poorly understood. Hamilton²⁷ reviews 2 interesting cases. The first, described by Grolnick in 1929, was that of a painter who intermittently for a period of two years used oxalic acid in cleaning floors without protecting his hands with rubber gloves. He experienced severe pain, stiffness and numbness of the fingers. Examination revealed deep cyanosis involving the fingers and hands to the wrists, the soft tissues were tense, the skin felt cold, and the nails were yellow in color. Recovery followed treatment with hot Epsom salt soaks, dry heat and woolen bandages. The second case was reported in 1939 by Howard.³⁰ This was the case of a man whose occupation involved the cleaning of automobile radiators. In this work he boiled parts in a strong solution of oxalic acid and consequently for a period of several months was heavily exposed to oxalic acid fumes. In addition, he frequently handled oxalic acid crystals with his bare hands. His symptoms were referable to the respiratory, gastrointestinal and central nervous systems. There were a metallic taste in the mouth, marked irritation of the eyes and throat, frequent epistaxes, severe headaches, repeated vomiting, persistent cough, productive at times of fragments of tissue, melena, severe low-back pain, loss of weight, muscular weakness and albuminuria. Recovery was slow, and a state of extreme nervousness persisted for a long period.

Acute poisoning develops within a few minutes to several hours after the ingestion of oxalate. The range of the lethal doses is extremely wide, values between 2 and 30 gm. of oxalic acid having been reported. Death is undoubtedly a result not

only of the quantity of acid consumed but also of other factors, such as the form in which the oxalate is consumed, the interval between consumption and therapy, the type of treatment, the condition of the patient prior to ingestion, the renal status and the gastric acidity. Death has occurred as early as three minutes and as late as fourteen days after ingestion. The symptoms of acute toxicity may be divided into those caused by a local corrosive action and those resulting from absorption and excretion of the soluble oxalate. If a high concentration or the solid form is taken, the local effects may be predominant and death may occur without development of symptoms dependent on absorption. Immediately on ingestion there is noted an extremely sour taste, followed by a violent sensation of burning in the mouth, pharynx and region of the stomach. There may be marked dysphagia and a sense of constriction in the throat. Within a few minutes retching and vomiting occur, the vomitus is described as being coffee-ground in color or dark red. Vomiting may become intractable and be followed by severe diarrhea, with or without melena. If the condition is untreated, the vomiting and diarrhea persist and the patient may die from dehydration and exhaustion.

If death does not result from collapse associated with acute hemorrhagic gastroenteritis, symptoms develop from the systemic effects and from renal insufficiency. The former are related to the depressing action of oxalate on the blood calcium,²⁴ by which it is rendered nonavailable, and possibly to some direct toxic effect on tissue cells.

It has been estimated that approximately 0.6 gm of oxalic acid in the human blood stream at one time is equivalent to the blood calcium.⁵ The cardiovascular, neuromuscular and central nervous systems are markedly affected. The skin is pale, cold and clammy, the pulse is weak or imperceptible, and the blood pressure and temperature are low. Numbness and tingling may develop in the extremities. Cramplike muscular and abdominal pain may be extremely severe. An erythematous rash has been noted. Local or generalized muscular twitchings occur and may progress to marked tetany and convulsive seizures. The tetany of oxalic acid poisoning is due to acute calcium deficiency and can be relieved by the intravenous administration of calcium salts. The central nervous system may show evidence of excitation or depression varying from an acute maniacal state to stupor and coma. Death results from cardiovascular collapse or depression of the central nervous system.

Renal involvement is frequent and, even if the patient survives the severe local and systemic effects, may be responsible for a fatal outcome. Renal insufficiency dominates the picture from the second day.²¹ Oliguria develops and may progress to anuria. The blood nonprotein nitrogen rapidly rises. Examination of the urine shows albuminuria, numer-

ous epithelial cells, hyaline and epithelial-cell casts, erythrocytes and calcium oxalate crystals. If anuria does not develop, oliguria is followed by polyuria and hyposthenuria, which may persist for a long period. If anuria occurs early or the onset of polyuria is delayed, the prognosis is poor.

The treatment of oxalic acid poisoning consists of repeated gastric lavage with lime water, intravenous calcium gluconate or chloride and supportive therapy directed toward maintenance of the fluid balance, an adequate renal output and a normal blood pressure.

Acute oxalic acid poisoning has been reproduced experimentally in animals. MacKenzie and McCollum¹⁹ in rats, Rost³¹ and Heubner and Hüchel³² in dogs and Baudouin et al.³³⁻³⁴ in rabbits and dogs have duplicated the sequence of events that occurs in cases of human poisoning. The depression of blood calcium has been verified,³⁴⁻³⁶ and some evidence has been obtained that the severity of the reaction is controlled in part by the parathyroid glands.³⁶

Considerable attention has been focused on the pathologic lesions developing in the kidneys of animals used in experiments involving acute and chronic oxalic acid poisoning. Dunn et al.³⁷ reviewed the literature and reported their own results in rabbits. The severity and reversibility of the damage varied with the amount of oxalate injected. The kidneys were swollen, pale and edematous. Marked necrosis, especially of the proximal convoluted tubules, occurred. Although occlusion of some of the renal tubules by calcium oxalate crystals was noted, this did not appear to be an essential feature of the nephritis. Gough³⁸ studied the mitochondria of the renal tubular epithelial cells and was able to demonstrate by his technic that even quantities of oxalic acid well below toxic doses cause cellular changes, which, however, were reversible. On the other hand, as the dose is increased nonreversible necrotic changes develop, which are detectable by ordinary histologic procedures. Most authors³²⁻³⁹ agree that the glomeruli are unaffected but that the epithelial cells of the convoluted tubules become swollen and necrotic. Calcium oxalate crystals have been demonstrated within the lumens of the renal tubules as well as within the epithelial cells. Heubner and Hüchel³² noted that at autopsy the *testes* showed the largest oxalate content of any organ and that examination of tissue sections by means of polarized light showed a wide distribution of crystals throughout the kidney. Koch²⁴ in a study of the kidneys of a fatal human case also was able to demonstrate intracellular oxalate crystals. Attempts to produce macroscopic oxalate calculi have not been highly successful. Rost,³¹ however, reported oxalate concretions in the calyces of the kidneys of three dogs fed sodium oxalate for several months and Kevser⁴⁰⁻⁴¹ was able on a few occasions to produce renal calculi in rabbits after

the administration of large amounts of butyl oxalate with calcium chloride or oxamide

Koch²⁴ concluded from his experiments that the type of renal damage depends on a number of variables, the most important of which is the nature of the oxalate excreted. Thus, if sufficient oxalic acid or soluble oxalate reaches the kidney a necrotizing nephritis may result, whereas if absorption has been slow and sufficient time has elapsed for complete combination with calcium, the results depend on the hypersecretion of a normal urinary constituent

RHUBARB POISONING

From time to time there have appeared in the medical literature references to episodes of acute illness following the ingestion of rhubarb, particularly the leaves, and certain other foods—for example, sorrel⁴²⁻⁵⁰. The knowledge that such food-stuffs have a high oxalic acid content has invariably led to the incrimination of oxalic acid as the toxic factor in these cases. For instance, Widmark and Ahlén⁵ report that the stalks of rhubarb plants contain 0.39 to 0.51 per cent oxalic acid, whereas the leaves contain only 1.2 per cent. Other authors report comparable values

Beattie,⁵¹ in this country, in a government pamphlet issued in 1937, discussed this problem in these words

The succulent acid leafstalks of rhubarb make most excellent sauces and pies, and the question often arises about the use of the leaf blades for greens. Numerous cases of more or less serious illness and some fatalities have been reported in both Europe and in North America from eating rhubarb leaves. These leaf blades were eaten boiled in the belief that they were a suitable substitute for the common greens, but owing to the high content of oxalic acid and its soluble salts found in rhubarb leaves it is recommended that they be left entirely alone and not used under any circumstances as food. In the stalks, however, the oxalic acid is present in smaller amount and largely in insoluble form, and for this reason is harmless

This subject has also, in recent years, received editorial comment in the *Journal of the American Medical Association*⁵²

As reported in the literature the symptoms of rhubarb poisoning varied greatly. In mild cases the symptoms are those of a gastroenteritis, with abdominal pain, vomiting—occasionally with hematemesis—and diarrhea predominant. In severer cases, hemorrhagic diathesis, kidney, hematuria, convulsions, collapse, and coagulability of the blood and coma have been noted. At times, genitourinary symptoms—renal colic with hematuria—without gastrointestinal manifestations have been observed

Almost all the reported cases are in the earlier literature. Many occurred in England during World War I, at which time it had been suggested by various newspapers that rhubarb leaves be used as a vegetable substitute. The role of oxalic acid in some of the reported cases of rhubarb poisoning

is open to question. At times the amount of rhubarb consumed scarcely seemed likely to contain enough oxalic acid to be poisonous. Kohman¹ refers to an investigation by Maue in which he and five other men repeatedly ingested cooked rhubarb leaves with no toxic effects whatsoever. Other reports indicate that a food rich in oxalic acid was responsible for death or illness.⁵⁰ In one case death occurred after ingestion of half a peck of cooked rhubarb leaves and part of the water in which it had been cooked.⁵⁰ On investigation of an outbreak of "ptomaine poisoning" following the ingestion of soup of sour grass (sorrel), a public health official found that the soup contained about 0.13 per cent oxalic acid. The precise minimal amount of oxalic acid necessary to produce symptoms is not known, and perhaps varies with individual susceptibility and gastric acidity

It is well to remember that the gastroenteritis of food infection may readily simulate mild oxalic acid poisoning, and conversely that the abdominal pain, vomiting and diarrhea due to the ingestion of oxalic acid may simulate the gastroenteritis or gastritis of food infection. Since some skepticism has been expressed about this subject, physicians who encounter suspected cases of rhubarb poisoning could make a worth-while contribution to the medical literature by reporting cases that have been carefully studied by modern chemical and bacteriologic methods. There is a distinct paucity of reliable information on this subject in the modern literature

It is known that ingestion of an ordinary portion of cooked rhubarb stalks may cause an increase in the urinary excretion of oxalate.⁴⁴ In a susceptible person this may occasionally be the contributing factor in the production of clinically significant oxaluria. There are a number of reports of hematuria attributed to the ingestion of rhubarb.^{47, 48}

THE SYNDROME OF OXALURIA AND OXALEMIA

The identification of crystals of calcium oxalate in the urine by Donné in 1838 stimulated interest in their clinical significance. Within the following decade attempts were made to correlate the presence of the crystals with the occurrence of definite symptoms and signs, and under the influence of Prout, Golding Bird and Begbie,⁵⁴ there emerged the concept of a so-called "oxalic acid diathesis." Subsequently an extensive literature developed and such terms as "syndrome of oxaluria," "oxalemia," "oxalic acid diathesis" and "oxalic gout" became diagnostic scrap baskets. The German literature is conspicuous for the paucity of reports on this subject. A few papers have appeared in the English and American journals, but the greatest source of information has been the work of French and Italian investigators, who, it would seem, have been unduly influenced at times by the great European spas

The terms "oxalemia" and "oxaluria" refer to a state in which the oxalic acid levels of the blood and urine respectively are elevated above normal. Such elevated values have been reported in a wide variety of diseases, for example, diabetes, acute and chronic renal insufficiency, cirrhosis of the liver, nutritional deficiencies and cardiac failure. In addition to these well-recognized clinical conditions, oxalemia and oxaluria are said to be found in association with a variety of symptoms and signs that, grouped together, have been considered as a specific syndrome. The variations in the manifestations of this syndrome are numerous. It may mimic an acute abdominal crisis or biliary or renal colic, it simulates gastrointestinal or genitourinary disease, it presents itself as a disease of the muscles or joints, or it manifests itself as a disease of the central nervous system.

Neville⁵⁵ and Goffon and Nepveux⁵⁶ refer to a constitutional diathesis associated with the syndrome. The patient is irritable, depressed, anxious, hypochondriacal, dyspeptic and neurasthenic. In addition, he may show periodically one or any combination of the following clinical pictures.

The gastrointestinal tract may be, and frequently is, the site of greatest disturbance.⁵⁷⁻⁶⁰ There may be epigastric distress after eating, diarrhea alternating with constipation, severe gastric crises with retching, vomiting, even hematemesis and spasmodic intestinal pain, which may be accompanied by the passage of calculi or blood from the rectum. The vomitus has been reported to contain calcium oxalate crystals.⁵⁷ The abdominal pain may be extremely severe and associated with signs of an acute intestinal obstruction. A description of 2 such cases, one of which was subjected to abdominal exploration, was reported by Rawling.⁶¹ These, however, appear to have been cases of oxalate lithiasis with marked gastrointestinal symptoms and need not be designated as a special syndrome.

A second manifestation of the syndrome is renal in nature. The literature contains a number of reports of severe renal episodes thought to be examples of the syndrome.⁶²⁻⁷¹ In general, the picture is that of severe renal colic, either unilateral or bilateral. There is pain in the flank, which may radiate to the genitalia, frequency, urgency, burning on urination, cystalgia and gross and microscopic hematuria. Reflex gastrointestinal symptoms—vomiting, abdominal distention and so forth—may occur. The episodes are paroxysmal and at times appear to have a tendency toward a seasonal recurrence, being most prominent during the summer. In some reports this has been attributed to the consumption of such foods as rhubarb, spinach, tomatoes, strawberries and gooseberries, foods thought to be rich in oxalates, others attribute it to the precipitation of calcium oxalate crystals because of concentration of the urine during the warm weather. Most of the reported assays, how-

ever, fail to confirm high oxalate values in any but the first two mentioned foods. Examination of the urine at the time of the attacks reveals a heavy concentration of calcium oxalate crystals, irritation from which is the explanation for the pain and hematuria. Roentgen-ray and cystoscopic examinations have been negative in the cases in which studies have been made. The symptoms are said to disappear when the patient is maintained on a low oxalate diet and fluids are forced. The renal manifestations of the syndrome appear to be the best substantiated. The most modern support to the theory that oxaluria may produce symptoms has been given by Black.⁶⁸ Oxaluria with symptoms—chiefly colic and hematuria—occurred in 43 men and was the most frequent urologic condition requiring hospital admission among soldiers from a British division training in India. In this study oxaluria was not diagnosed until a full investigation—cytologic and bacteriologic examination of the urine, cystoscopy and intravenous or retrograde pyelography—had been carried out to exclude other causes for these symptoms. Black also presented some cases suggesting that oxaluria with epididymitis may be a distinct entity.

Loeper,⁷² Loeper et al.⁷³ and Violle⁵⁹ use the term "oxalic acid gout" to designate a condition in which the oxaluric diathesis is accompanied by symptoms and signs associated with the muscles or joints. They claim that patients with this ailment have oxalemia with a variety of findings, for example, migraine headaches, psychasthenic depression, vague pains, hypotension, gastric and intestinal crises, mucous colitis, intestinal and renal lithiasis and hematuria. In addition, they have severe chronic rheumatism and arthritis and may develop a tophaceous type of "gout." The rheumatism is described as an afebrile, slowly progressive, chronic disease. There are vague pains in the extremities and fingers, with crepitation of the knees and shoulders. Enlargement of the ends of the phalangeal bones occurs, and knotty deformities the size of lentils may develop on the lateral aspects. Sometimes mild dislocations occur. On roentgenologic examination the bones appear to be rarefied, and there is thickening of the periarticular tissues, deformities of the phalanges and erosions of the ends of the bones. The tophi, when present, are aberrant, juxta-articular or articular in location. It is thought that originally the tophi are primarily pure calcium oxalate, but that eventually they change to calcium carbonate or are followed by the precipitation of cholesterol and uric acid so that mixed tophi result. Loeper⁷² claims that the administration to a patient of this type of calcium oxalate or foods rich in oxalates causes an exacerbation of the symptoms.

Grott⁷⁴ reported 4 cases of acute arthritis clinically indistinguishable from acute gouty arthritis. When the patients failed to respond to the routine therapy for gout, determinations of blood uric acid

and oxalic acid showed the former to be normal and the latter elevated. Clinical improvement followed administration of diets low in oxalates. Dietary indiscretions were frequently followed by exacerbations of symptoms. Grott concluded that some cases of gouty arthritis are related to disturbances in oxalic acid metabolism rather than to those in uric acid metabolism. This concept has not been confirmed.

Cohen and Reid⁷⁶ reported 7 cases of tenosynovitis crepitans involving the flexor and extensor tendons of the wrist. Although it was true that in most cases mechanical strain appeared to be a precipitating factor, oxaluria occurred in every case, and in 3 cases there was in addition a history of urinary lithiasis. There was no response to the usual therapy until a regime of low-oxalate diet, alkalization and increased intake of magnesium was instituted.

Laroche⁷⁶ has summarized the clinical picture of oxalemia with involvement of the central nervous system. Asthenia, melancholia and vague pains have been noted. Migraine attacks are frequent. Intercostal, crural, sciatic and brachial neuralgia may predominate. Convulsive seizures have been reported by Rodillon⁷⁷ in patients whose spinal fluids contained crystals of oxalic acid. Finck⁷⁸ reported the case of a patient with severe headache and the signs of marked meningeal irritation. The condition persisted until the onset of hematuria associated with marked oxaluria, following which the neurologic picture completely disappeared.

In its complete form this syndrome apparently mimics a wide variety of clinical pictures. The mechanisms suggested to explain it are largely speculative and, except for the renal phase, remain for the most part as obscure as the so-called "facts" related to the intermediary metabolism of oxalates.

The syndrome of oxaluria with colic and hematuria is often mentioned in the American literature and in textbooks on urology. There appears to be a growing appreciation of the fact that renal colic and hematuria may result from the passage of crystals or microscopic aggregates of crystals as well as from macroscopic stones. For example, sulfonamide therapy may give rise to it. Less known but well described in the literature is the syndrome of uric acid showers with renal colic.⁷⁹⁻⁸¹ Uric acid crystals may precipitate out, irritating the renal pelvis and ureter and producing colic. They redissolve before voiding. The patient passes very acid urine, generally clear of crystals but containing red blood cells. If the urine is allowed to stand for twenty-four to seventy-two hours in a sterile test tube, crystals precipitate on the glass and on tapping the tube rain to the bottom and may be collected for microscopic and chemical analysis.

A large municipal hospital like the Boston City Hospital receives many emergency admissions for renal colic. We have been impressed over the

years with the frequency with which the standard K U B (kidneys, ureters and bladder) roentgenogram and routine pyelogram, when used alone, fail to demonstrate a calculus or to establish the cause of the colic. It is well for the physician to keep in mind that the clinical picture of renal colic without a demonstrable calculus on a K U B roentgenogram may be due to a non-shadow-producing calculus or mass, — uric acid, fibrin or blood clot, — Dietl's crisis, sulfonamide lithiasis, oxaluria, syndrome of uric acid showers, possibly the passage of excessively concentrated urine and so forth. Patients admitted to a hospital for renal colic should be instructed to void each specimen of urine into a urinal through a piece of cloth. Not only does the recovery of some gravel or a stone establish the diagnosis, but chemical analysis indicates the nature of the calculus and enables the physician to plan a more rational method of therapy. Urine voided during or shortly after an attack of colic should be examined for crystals as well as other sediment, the specific gravity and the pH. Red blood cells disappear if urine stands too long or is too dilute. If the urine is extremely acid a specimen in a sterile test tube should be set aside for precipitation of uric acid crystals. A chemical test for cystinuria, the Sulkowitch test for hypercalciuria and culture of urine for urea-splitting organisms are well within the scope of any hospital laboratory. These procedures often enable the cause of renal colic to be established when calculi are not detected by roentgen-ray study.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31331

PRESENTATION OF CASE

A fifty-nine-year-old woman was admitted to the hospital complaining of a mass in the abdomen.

Ten months before admission the patient noticed, after reaching forward, a sensation of heaviness in the abdomen occurring about once a month and followed on one occasion by watery diarrhea. Four months later, while lying on her right side, she detected a mass in the left flank that progressively increased in size but caused no symptoms, except a sensation of weight, at times it seemed to pulsate. Two months before admission she had an attack of low back pain, which radiated upward and was severer than the back pains that she had had for many years. During this period she worked hard and became weak, tired and dyspneic, after a period of rest these symptoms disappeared.

The past history was noncontributory except that she had been jaundiced for one month thirty years previous to admission.

On examination the patient was a well developed, moderately obese woman in no acute discomfort. Multiple subcutaneous nodules were palpable over the arms and thighs. The heart and lungs were normal. In the left upper quadrant of the abdomen was a firm, moderately tender, irregular mass about 10 cm in diameter. It descended with inspiration and was movable on pressure in the left costovertebral angle. Peristaltic sounds were heard in the region of the mass. Pelvic and rectal examinations were negative.

The temperature, pulse and respirations were normal. The blood pressure was 125 systolic, 80 diastolic.

Blood examination showed 14.9 gm of hemoglobin and a white-cell count of 7400. The stools were negative for occult blood. The nonprotein nitrogen was 15 mg per 100 cc, and the fasting blood sugar 100 mg. The total serum protein was 6.1 gm per 100 cc. The serum amylase was 36 units per 100 cc. All urine specimens were negative.

A barium enema done ten days before admission showed passage of barium from rectum to cecum without delay. There was reflux into a normal

appearing terminal ileum. No constant filling defect, ulceration or diverticulum was seen in the colon. The ascending colon and cecum were twisted on themselves so that the tip of the cecum lay in essentially the same position as the hepatic flexure. The palpable mass in the left upper quadrant was not attached to the bowel (Fig 1). It displaced the splenic flexure laterally, and the transverse colon inferiorly. The palpable mass was distinctly seen on the film. It measured 10 cm in diameter. The stomach appeared to lie medially to the mass and above it. The spleen was not visualized. A small bowel enema showed the mass to lie in the left upper quadrant, between the stomach and transverse colon, displacing the stomach upward and the transverse colon and upper small intestine downward. An intra venous pyelogram was negative. A gastrointestinal series was negative.

On the ninth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR MERRILL C. SOSMAN†: I should like to have more details about the nodules found over the arms and thighs. How large were they? Were they freely movable? What was their distribution? Was there any pigmentation associated with them? I assume that they were neurofibromas.

DR BENJAMIN CASTLEMAN: There is no further information recorded. I should agree that they were probably neurofibromas.

DR SOSMAN: "The heart and lungs were normal." I assume that statement was based on the usual method of examination with the stethoscope, which is not reliable in spite of what one of your doctors said at one of these meetings several months ago. Since there are no x-ray films of the chest, we must accept the opinion, but not as a fact.

The serum amylase was 36 units per 100 cc. At the Peter Bent Brigham Hospital anything up to 100 units is normal. This was well below the border line of abnormality.

Submitted with this protocol was this series of x-ray films. There are several facts that can be determined from the x-ray studies, and opinions can be deduced from these facts. I think that we should carefully separate the two. First there is a barium enema, then a small-bowel study, then intravenous urograms, and finally, a gastrointestinal series. I was a little intrigued in going over these films to find that all of them have the same identifying number but one. I assume that you have a unit number for these patients, and I wonder if this film belongs to the group.

DR DEAN CRYSTAL: The patient was seen in the Out Patient Department and given a number, and was then transferred to the house and given another

†Clinical professor of radiology, Harvard Medical School, radiologist, Peter Bent Brigham Hospital.

*Case records of the Massachusetts General Hospital (Case 31322). *New Eng J Med* 232:353-358, 1945.

number before it was realized that she was the same patient

DR SOSMAN We can check that statement by observing the details of the spine — the intimate, personal, private anatomic details. As a matter of fact, x-ray films are a good method of identifying persons during life and even after death, and they have frequently been used for that purpose. If one compares the transverse processes, the articular facets

upward. There is a large vacant area here, which spreads the duodenal loop. It looks as if the mass had moved to the right side. I cannot tie that up with the examination when it was said that the mass was in the left upper quadrant. I should like to ask if the mass moved.

DR LAURENCE L. ROBBINS Dr H. P. Mueller, who did the fluoroscopy, — in fact, I believe that he interpreted all the films, — was certain that each



FIGURE 1 Roentgenogram of the Abdomen Showing the Soft-Tissue Mass in the Left Upper Quadrant

and the details of the fourth and fifth lumbar vertebrae in these films one finds that they are identical, so that the statement is correct.

The outline of the mass is best seen in this film of the kidney and bladder region, which preceded the intravenous urogram. There is a fairly sharply outlined mass in the left upper quadrant, which also shows well in the barium-enema film. The protocol states that the mass was irregular to palpation, whereas the shadow on the x-ray film is smooth and distinct in outline, making it look like a cystic mass. I agree, however, with the report that the first barium enema was normal. There is no evidence that the tumor arose from the colon. The stomach is displaced

time he examined the patient the mass was in a different part of the abdomen.

DR SOSMAN So it was a freely movable mass, and I assume that the mass in the right upper quadrant below the antrum of the stomach, lying above the colon and distending the duodenal loop (Fig 2), is the same one that we saw in the left upper quadrant (Fig 1).

The intravenous urogram is essentially normal, except that the upper calyces of the left kidney are not well filled. There are two small areas of calcification that might be interpreted as the tips of these calyces, since they are in proper relation to the outline of the kidney. As a matter of fact, the

two shadows are present in the plain film before the intravenous urogram was made. I assume that these two small calcified areas were in the mass and were not part of the kidney.

Finally the gastrointestinal series shows a well filled stomach, with normal mucosa and normal peristaltic waves, and a normal duodenal loop. I consider this jejunal loop to be abnormal. It is a little too large, and the rugae on the left side adjacent to the mass are not entirely distinct. Going back to the small-bowel examination, I see a loop

it would probably have to be a large benign cyst) a cyst in the tail of the pancreas and, finally, an ovarian cyst with a long pedicle. These are the five major considerations. I believe that we can rule out the spleen because the tumor does not displace the colon in the usual manner. An enlarged spleen almost invariably displaces the splenic flexure downward and medially, whereas here the mass lies medial to the splenic flexure. If it is spleen, it would have to be an aberrant spleen, and presumably a tumor of an aberrant spleen.



FIGURE 2 Roentgenogram Showing the Mass Displacing both the Barium-Filled Stomach and the Colon
The mass has migrated to the right of the spine

of small bowel that I think is larger than one ordinarily sees.

To sum the whole thing up, the patient came in with a mass in the left upper quadrant, and after nine days of hospital study the diagnosis was still a mass in the left upper quadrant. I do not believe that there is any evidence here to indicate the exact origin of the mass. From these examinations, however, we do know that it was not a part of the stomach and that it did not arise from the colon, if this dilated loop of small bowel means anything, it could have arisen from the wall of ileum. We have to consider, then, a tumor of the small bowel, a mesenteric cyst, a tumor of the left kidney (with no more distortion of the renal pelvis than we have here,

Going back to the small bowel and jejunum, there are four or five conditions that are commonly found there. One is reduplication, which almost always is found in children. I believe that it is quite rare to see it in a woman of fifty-nine. Then there are the sarcomas, — leiomyosarcoma and spindle-cell tumors, — but in such cases there is almost invariably a history of ulceration and hemorrhage. This patient had no anemia and no blood in the stools. The episode of weakness, fatigue and dyspnea could have indicated a massive gastrointestinal hemorrhage, but she failed to notice tarry stools. Lymphoma is frequently found in the small bowel, but that also is likely to cause hemorrhage, although not so often as the spindle-cell sarcoma, further

ore, there is usually evidence of the disease elsewhere. Finally, we must consider a neurofibroma arising in the wall of the bowel or one of the nerves in the mesentery. She had subcutaneous neurobromas, but I do not remember ever having seen a large neurofibroma in the abdomen. This is still a possibility in spite of that.

Mesenteric cysts are fairly rare. A cyst of unknown etiology with chylous fluid or serous fluid is occasionally seen. And there are the so-called "enteric cysts", the pathologists give them this name, but they are probably the same as the reduplications that they talk about at the Children's Hospital. There are also the extremely rare nephrogenic cysts, which occur in the bowel remnants of the wolffian body, and a dermoid cyst, not associated with the ovary, is occasionally found. In fact, the two areas of calcification are suggestive of the latter.

I do not believe that it was a cyst of the pancreas because it was so freely movable and because of its location. It could have been a cyst of the ovary with a long pedicle, and that might account for the severe attack of pain in the back radiating upward, assuming that the previous ones that she had had many times were from the same cause. That would nicely explain the pains — torsion of an ovarian cyst with a long pedicle.

After looking over all these possibilities, I have no particular opinion concerning what it really was. I have ruled out a good many things, but there are still some even more remote possibilities, such as carcinoid of the small bowel or argentaffin tumors. These are found in association with multiple neurofibromas, but the carcinoid or argentaffin tumor is extremely small and rarely undergoes cystic degeneration, in all probability it can be ruled out. I have narrowed the field down to two main possibilities — ovarian cyst with a long pedicle and enteric cyst in the wall of the small bowel. Ovarian cyst must be considered, particularly because of the remarkable mobility of the mass. I believe that we can rule out cyst of the kidney. If this is the same tumor on the right, we can rule out cyst of the pancreas. I shall have to make a double-barreled diagnosis, so to speak, instead of pinning all my faith on a single one, that is, enteric cyst or ovarian cyst.

DR ROBBINS: We followed the same line of reasoning as Dr Sosman. I do not believe that we were impressed with the appearance of the jejunum. Dr Mueller said that during fluoroscopy the jejunum appeared to be normal. I thought that it probably was a cyst in the gastrocolic ligament because of the way it so consistently maintained its relation to the colon and stomach.

CLINICAL DIAGNOSIS

Pancreatic cyst.

DR SOSMAN'S DIAGNOSIS

Enteric or ovarian cyst

ANATOMICAL DIAGNOSIS

Multilocular cystoma of pancreas

PATHOLOGICAL DISCUSSION

DR CASTLEMAN: Dr Crystal, will you tell us what you found at operation?

DR CRYSTAL: We found a large tumor with a granular surface pushing the gastrocolic ligament forward. It proved to be a huge multilocular tumor of the neck of the pancreas, the portion that lies to the left of the notch for the mesenteric vessels. A small part of the mass was attached to the region just to the left of the mesenteric vessels. It could



FIGURE 3 Photograph of a Cross Section of the Specimen

not be dissected free from the pancreas, and yet it appeared to be an encapsulated benign tumor. It was possible to transect the pancreas in two places, one just to the left of the uncinate notch and the other just to the left of the tumor, at a distance of about 5 cm, and to lift the tumor out, preserving intact the splenic vessels, which we did not have to tie. The question then rose whether or not we should remove the tail of the pancreas and the spleen along with the tumor. We elected to leave the pancreas and spleen, the latter was done because of our observation on several occasions that incidental removal of the spleen has been followed by thrombosis of the splenic vein.

The patient has done well. I do not know whether she will develop a pancreatic fistula. She has had fever every day, and I imagine that a fistula may eventually appear, possibly lasting for several months.

DR CASTLEMAN: The mass that we received was well encapsulated and quite nodular, but the nodules were smooth, not granular such as one may

see in ovarian carcinoma. These nodular areas were translucent, pinkish and gelatinous, being quite similar in appearance to the thyroid tissue. A cross section of the tumor revealed varying sized multilocular cysts filled with viscid gelatinous semisolid material resembling colloid (Fig 3).

Histologically one section showed a bit of pancreatic tissue separated from the tumor by a thick

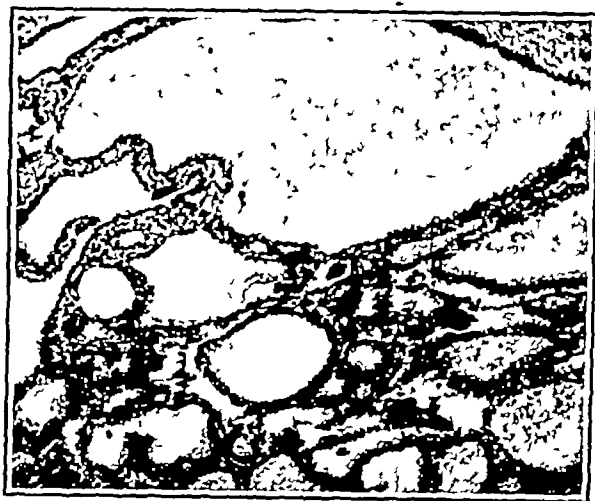


FIGURE 4 Photomicrograph Showing the Cystic Spaces

capsule. The mass was made up of cysts of varying sizes, separated by fibrous connective tissue (Fig 4). The lining of these cysts was flat to low cuboidal epithelium, and occasionally there was a suggestion of papillary projections. This is the appearance that we have seen a number of times in so-called "cysts of the pancreas." I believe that the lining is epithelial, although it is conceivable that it is endothelial, the tumor being a form of lymphangioma. Although they are often called "cystadenomas," I prefer the term "cystoma" because they really do not form glands. They are simply spaces with single layers of epithelium, occasionally high and with a papillary arrangement. There was no evidence of malignancy.

CASE 31332

PRESENTATION OF CASE

A forty-nine-year-old woman was admitted to the hospital complaining of dyspnea and a sensation of pressure over the sternum.

During the year before admission the patient had had a marked decrease in appetite and had lost 20 pounds in weight. During the same period her teeth had rapidly become carious. Six months before entry she first noted swelling of the ankles and feet, worse at night and accompanied by aching from the hips downward. Exertional dyspnea soon developed, and she became easily fatigued. Early

in her illness she complained of pain in the shoulders and arms, usually on the right but sometimes on the left. She consulted a physician, who found albumin in the urine. At that time the red-cell count was 5,000,000. Weakness and fatigue progressed, and she became extremely pale. The red-cell count was found to have decreased to 2,000,000. Liver and iron were given, with improvement of the pallor but not of strength. For nine weeks before admission she was confined to bed. Each evening there was a low-grade fever, the highest temperature recorded being 101°F. Chest plates taken two months before admission were said to have shown healed tuberculous lesions in both lung fields. Two days before admission the patient first experienced an attack of breathlessness, with a sensation of extreme sternal pressure from the xiphoid to the sternal notch, tickling in the throat and a dry spasmodic nonproductive cough, accentuated in the sitting position. There was no chest pain. These symptoms persisted, and respiration was difficult. Orthopnea appeared, with palpitation and sweating. She could not sleep well, and sedatives had been given.

Before the onset of her illness the patient's health had been excellent. One brother had died of tuberculosis, and another brother and a sister had active tuberculosis at the time of the patient's admission.

Physical examination revealed a markedly pale, acutely ill, apprehensive woman, gasping for breath. Purplish blotches were seen about the wrists and ankles. The pupils and fundi were normal. The teeth were markedly carious, with pyorrhea. The tongue was smooth, with no lesions. The cervical, axillary and inguinal nodes were firm, shotty and nontender. The thoracic cage was poorly developed, and the xiphoid depressed. Breathing was chiefly abdominal, without lag or retraction. Over the right upper chest, posteriorly, tenderness was elicited and expiratory wheezes were heard. The mediastinum was widened, extending 15 cm on each side of the midline. The point of maximum cardiac impulse was 8 cm to the left of the midline. A harsh systolic murmur was heard over the entire precordium. The abdomen was spastic. The edge of the liver was percussed four fingerbreadths below the right costal margin, but satisfactory palpation was impossible. The spleen could not be felt. The reflexes were physiologic.

The temperature was 100°F, the pulse 100, and the respirations 25. The blood pressure was 210 systolic, 100 diastolic.

Examination of the blood showed a red-cell count of 2,090,000, with 51 gm of hemoglobin, and a white-cell count of 13,100, with 85 per cent neutrophils, 7 per cent lymphocytes, 5 per cent monocytes and 3 per cent basophils.

X-ray examination of the chest showed an extensive old tuberculous process, there were mottled areas of increased density and interspersed fibrosis occupying the upper two thirds of both lung fields and

extending into the right lower lung. There seemed to be a cavity in the right upper chest, and probably many small areas of cavitation in both upper lobes, the so-called "bronchiectatic changes" of long-standing tuberculosis. The remaining, better ventilated portions of the lung showed a hazy increase in density.

The temperature varied from 100 to 101.5°F, falling to 97 terminally. The patient went downhill rapidly and expired on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR WILLIAM W. BECKMAN: There are probably two unrelated parts to this illness—first, the pulmonary disease, which was apparent by x-ray examination, and second, the remainder of the illness—the debility, the edema, the albuminuria, the rapidly progressing refractory anemia, the hypertension and the terminal episode, which is consistent with left ventricular failure in a hypertensive heart. That train of events led me to believe that it was necessary to make a diagnosis of nephritis. The question is what kind of nephritis. One can fairly well rule out malignant hypertension by the fact that the eyegrounds were normal. Between chronic glomerulonephritis and chronic pyelonephritis it is impossible to differentiate without more information regarding the urine than is provided in this protocol. Either might have accounted for the symptoms.

An attractive possibility is periarteritis nodosa, which can, of course, produce nephritis with albuminuria and hypertension, and which would explain some of the other findings that are difficult to account for, such as the skeletal symptoms that she experienced from time to time. These were vague, and I do not know how to interpret them, but vague skeletal symptoms are said to be a feature of periarteritis nodosa. I might say parenthetically that there are two types of periarteritis nodosa: one occurs incidentally along with other conditions, such as hypersensitivity, and the second causes the clinical syndrome of periarteritis nodosa. The latter, which I am incriminating here, is characterized by an insidious onset, with debility, weight loss and symptoms referable to the vascular system. There are vague skeletal pains, as I have said, and also lesions that are compatible with the description of those over the wrists and ankles in this patient. I am afraid, however, that there is not enough evidence here to make a diagnosis of periarteritis nodosa. In the first place, one expects to find eosinophilia, and there was not even a single eosinophil in the blood smear. In the second place, I rather suspect that, if she had died of periarteritis nodosa, she would have had a good many more symptoms referable to the vascular system, such as abdominal pain, pain in the extremities similar to intermittent claudication, cerebral phenomena and so forth. She had none of these, and it is im-

probable that she had periarteritis nodosa. I say that particularly because every time I discuss one of these cases I make that diagnosis and it is always wrong.

Before I go farther with the discussion I should like to see the x-ray films.

DR MILFORD D. SCHULZ: The films show what is stated in the protocol.

DR BECKMAN: Undoubtedly, but I do not understand what the protocol said.

DR SCHULZ: The films show fibrous lesions involving the apices. There seems to be something else going on, as shown by the areas of increased density extending from both hilar regions. Several rounded areas of increased density are seen in the lower portions of the lungs. One almost looks as if it had a fluid level.

DR BECKMAN: Could she have had pulmonary infarction?

DR SCHULZ: I wonder if she could have had multiple septic pulmonary emboli in addition to the old disease. The hilar vessels are rather prominent, but there does not seem to be pleural effusion. The heart is enlarged, and there is some prominence in the left auricular area. Calcification in the valves is not apparent.

DR BECKMAN: I still do not know what this patient had. She seems to have had an old pulmonary tuberculosis. I suppose that whether or not this was active cannot be told from the chest films, and in the absence of a sputum examination I cannot decide whether she had an active pulmonary tuberculosis. If it were active, it would account for the low-grade fever that she was running.

If one were to attempt to relate the whole picture,—the pulmonary and the renal disease,—I should think that one would have to bring in the possibility of chronic pulmonary sepsis—tuberculosis or some other disease—leading to amyloidosis, including amyloid kidneys, and thereby causing the train of events that took place. I do not have any way of establishing that diagnosis either, but it is unlikely in view of the high blood pressure, which is not frequent in renal amyloidosis. As a matter of fact, I can mention a lot of things but cannot establish any of them. As I have said, the terminal episode might have been due to left ventricular failure. The abrupt onset of breathlessness is consistent with that. It is rare, however, to have a marked feeling of substernal oppression in that syndrome. Although these patients sometimes complain of precordial discomfort, what this patient experienced is more than usual, and I wonder whether she might have had a large pulmonary embolus two days before admission to the hospital, which was the final cause of her death. I do not believe that I can settle any of these questions.

It seems likeliest that this patient had nephritis, either chronic glomerulonephritis or chronic pyelonephritis. There is no way of differentiating these

two, but I will bet on glomerulonephritis, with resulting hypertension and hypertensive heart disease, left ventricular failure and pulmonary edema. She also had an old pulmonary tuberculosis, which was probably inactive.

A PHYSICIAN Is carcinoma of the lung of common occurrence in women and is it ever bilateral?

DR BENJAMIN CASTLEMAN Primary carcinoma of the lung is more frequent in men than in women, but it certainly does occur in the latter. It is almost always unilateral. When it is bilateral, the lesions on one side are usually metastases from the other side.

Dr Schulz, do these films suggest carcinoma?

DR SCHULZ I do not know how one could rule it out, but it does not have to be primary in the lung.

DR E D MASON I have never seen anything like the rash on the ankles and wrists. It resembled post-mortem lividity, and we could not explain it. It was hemorrhagic and deep purplish.

DR REED HARWOOD If this patient had left ventricular failure, is it not surprising that she did not have more x-ray evidence of pulmonary congestion?

A PHYSICIAN A large liver is usually associated with right ventricular failure, rather than with left ventricular failure. What explains the large liver?

DR BECKMAN I doubt that it was really enlarged. When the liver is described as large in such vague terms, it usually turns out not to be. Dr Castleman will settle this point later.

CLINICAL DIAGNOSIS

Pulmonary tuberculosis, active

DR BECKMAN'S DIAGNOSES

Chronic glomerulonephritis

Hypertensive heart disease, with left ventricular failure

Pulmonary edema

Pulmonary tuberculosis, probably inactive

ANATOMICAL DIAGNOSES

Subacute glomerulonephritis

Hemorrhagic pulmonary edema, severe

Bronchopneumonia

Cardiac hypertrophy, hypertensive type, slight

Periarteritis nodosa, focal bronchial lymph node and pancreas

Pulmonary tuberculosis, healed, apical

PATHOLOGICAL DISCUSSION

DR CASTLEMAN Autopsy showed a pair of lungs that were quite heavy, being two or three times the normal weight. There were no adhesions or fluid in either pleural cavity. On section we were unable to find any cavities. In the right lung there was an old tuberculous scar surrounded by compensatory emphysema. It is quite possible that this focal emphysema might have produced an x-ray picture simulating a cavity. This scar was the only evidence of tuberculosis that we could find. The rest of the lungs were boggy and soggy, being full of fluid and blood. Every alveolus was filled with either blood or fluid, and some of them contained polymorphonuclear cells. In other words, this was an extremely severe form of hemorrhagic edema, the type that is often seen in patients with renal disease and the type that was recognized roentgenologically a few years ago by Dr Richard Schatzki,* of our x-ray department.

We did find renal disease. Each kidney weighed about 100 gm, and although the surfaces were smooth, they were studded with petechial hemorrhages. In gross the prosector, Dr J P Kujala thought that there probably was a nephritis. Microscopically it proved to be subacute glomerulonephritis. It apparently had gone on to the chronic stage, because none of the glomeruli were completely hyalinized and there was no surface granularity. That fits in with the size of the heart, which weighed only 250 gm, although the left wall was slightly hypertrophied.

An interesting incidental finding, which will probably please Dr Beckman, was the presence of periarteritis in two vessels, one in a hilar lymph node and the other in the pancreas. The kidneys, however, showed no evidence of periarteritis nodosa. I have not been able to find out whether the patient had ever been given sulfonamides, the thought being that it might have been the result of an allergic reaction.

DR BECKMAN How large was the liver?

DR CASTLEMAN It was within normal limits, weighing 1500 gm.

*Scott, T. Schatzki, R. and Bauer, W. Pulmonary edema: its roentgenologic appearance in acute glomerulonephritis without signs of cardiac failure. *JAMA* 114:613, 1940.

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A M A PROGRAM

On page 224 is reprinted the platform that was adopted by the Council on Medical Education and Public Relations and the Board of Trustees of the American Medical Association on June 22 and that originally appeared in the July 21 issue of the *Journal of the American Medical Association*

Undoubtedly this program will do much to clarify the stand of the American Medical Association, and certainly the fulfillment of its principles would accomplish a great deal toward the improvement of medical care. On the other hand, it seems unfortunate that nothing is said regarding the promotion of co-operation and an improved understanding among groups and individuals concerned with the

provision of all types of medical care, that the political control or domination of medical practice is not denounced (rather than a plea being made for the "postponement of consideration of revolutionary changes"), that the need for additional and improved hospital facilities, particularly in rural areas, is ignored, that the necessity of providing adequate means for the postgraduate instruction of discharged medical officers and civilian physicians is disregarded, that the opportunities for advancement in the field of industrial medicine are not mentioned and, finally, that the possibilities connected with education of the public in matters pertaining to medicine, other than those concerned with voluntary insurance, are ignored. Anyone who is at all familiar with the activities of the American Medical Association appreciates that all these matters are receiving due attention, and why they were omitted from a statement purporting to present the ideas of the American Medical Association regarding ways and means for improving the health of the Nation is incomprehensible.

It is obvious that the American Medical Association can do little toward attaining the objectives of this platform. In other words, the program is a direct challenge to physicians and to the state agencies — medical societies, hospital associations, departments of health and so forth — that are involved in the provision of medical and hospital care. Much has to be done, and promptly, if Congress is to be convinced that the provisions contained in the Wagner-Murray Bill (S 1050) are ill advised and unnecessary.

"WHERE THERE IS NO VISION"

AFTER the war is over, according to the fixed beliefs of many people, — beliefs built firmly around their faith in the fulfillment of a personal wish, — many things will come to pass. Permanent peace will brood over the land, certainly so if our global friends and neighbors adopt our views on international matters, we shall return to the goodness of former days, separated in some mysterious manner from their evil, we shall have new radios, with television, wireless telephones so that we can

CONSTRUCTIVE PROGRAM FOR MEDICAL CARE

AMERICAN MEDICAL ASSOCIATION

This platform was adopted by the Council on Medical Service and Public Relations and the Board of Trustees of the American Medical Association on June 22, 1945

Preamble

The physicians of the United States are interested in extending to all people in all communities the best possible medical care. The Constitution of the United States, the Bill of Rights and the "American Way of Life" are diametrically opposed to regimentation or any form of totalitarianism. According to available evidence in surveys, most of the American people are not interested in testing in the United States experiments in medical care which have already failed in regimented countries.

The physicians of the United States, through the American Medical Association, have stressed repeatedly the necessity for extending to all corners of this great country the availability of aids for diagnosis and treatment, so that dependency will be minimized and independence will be stimulated. American private enterprise has won and is winning the greatest war in the world's history. Private enterprise and initiative manifested through research may conquer cancer, arthritis and other as yet unconquered scourges of humankind. Science, as history well demonstrates, prospers best when free and unshackled.

Program

The physicians represented by the American Medical Association propose the following constructive program for the extension of improved health and medical care to all the people:

- 1 Sustained production leading to better living conditions with improved housing, nutrition and sanitation which are fundamental to good health, we support progressive action toward achieving these objectives.
- 2 An extended program of disease prevention with the development or extension of organizations for public health service so that every part of our country will have such service, as rapidly as adequate personnel can be trained.
- 3 Increased hospitalization insurance on a voluntary basis.
- 4 The development in or extension to all localities of voluntary sickness insurance plans and provision for the extension of these plans to the needy under the principles already established by the American Medical Association.
- 5 The provision of hospitalization and medical care to the indigent by local authorities under voluntary hospital and sickness insurance plans.
- 6 A survey of each state by qualified individuals and agencies to establish the need for additional medical care.
- 7 Federal aid to states where definite need is demonstrated, to be administered by the proper local agencies of the states involved with the help and advice of the medical profession.
- 8 Extension of information on these plans to all the people with recognition that such voluntary programs need not involve increased taxation.
- 9 A continuous survey of all voluntary plans for hospitalization and illness to determine their adequacy in meeting needs and maintaining continuous improvement in quality of medical service.
- 10 Discharge of physicians from the armed services as rapidly as is consistent with the war effort in order to facilitate redistribution and relocation of physicians in areas needing physicians.
- 11 Increased availability of medical education to young men and women to provide a greater number of physicians for rural areas.
- 12 Postponement of consideration of revolutionary changes while 60,000 medical men are in the service voluntarily and while 12,000,000 men and women are in uniform to preserve the American democratic system of government.
- 13 Adoption of federal legislation to provide for adjustments in draft regulation which will permit students to prepare for and continue the study of medicine.
- 14 Study of postwar medical personnel requirements with special reference to the needs of the veterans' hospitals, the regular army, navy and United States Public Health Service.

be in constant touch with our offices while fishing, juicy steaks synthesized entirely from yeast and broiled over synthetic hickory coals, sun-warmed and air-conditioned plastic houses with electric blankets on every bed, and automobiles, swift as the wind, silent as a tropical night, low hung and streamlined to raindrop perfection, with scratch-proof finish and puncture-proof tires. (The last specification is particularly desirable since the wheels will be practically unapproachable.) These things are being virtually promised to us by the wizards of industry as our reward for toppling the statue of fascism from its pedestal and preparing the latter for the advent of a shapely goddess, holding in one hand a miniature Diesel engine and in the other a pair of run-proof nylon stockings.

We are issued a timely warning, however, by Arthur W. Stevens, president of the Automobile Safety Association, in a letter published by the *Boston Herald* on May 24. The contents of this letter should be of special interest to the physicians of the Nation, concerned as they are more in public health than in the not inconsiderable fees to be derived from the patching up of injuries resulting from automobile accidents. The majority of these accidents, according to Mr. Stevens's plausible premise, are invited by the design of the present passenger car, which places the driver halfway back toward the rear of the car, "shutting off his effective view of the road and its hazards with an exaggerated hood, wide-flung fenders and thick corner posts." If we continue with the same trends in design, he adds, our highway massacre of the past will be resumed and will achieve even more appalling heights.

Mr. Stevens, in concluding his letter, quotes from an authority who had acquired a reputation for wisdom a thousand years before our Christian era began, — King Solomon, — who once declared, "Where there is no vision the people perish." We trust that the automobile designers of the postwar period will take note of Solomon's words and apply them in a practical manner to their own peculiarly important profession. We have had enough of violent death. If cars cannot be both graceful and safe, then the designers should at least try to approach the latter goal.

We should like to make still another suggestion while in the mood. It should not be too difficult to meter automobile horns to a certain small number of sound seconds per month, when the allotted time for hornblowing has run out, the car is put off the road until a new period begins. It's worth dreaming about.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BRESNIHAN — Frank N. Bresnihan, M.D., of Cambridge, died July 29. He was in his fifty-ninth year.

Dr. Bresnihan received his degree from Tufts College Medical School in 1913. He was a fellow of the American Medical Association.

His brother survives.

JACOBSON — Nathan L. Jacobson, M.D., of Lynn, died July 13. He was in his sixty-first year.

Dr. Jacobson received his degree from Maryland Medical College, Baltimore, in 1910. He was on the staffs of the Lynn and Union hospitals. He was a member of the Lynn Medical Association and the North Shore Medical Fraternity.

His widow, a son and a stepson survive.

RICHARDSON — Carl E. Richardson, M.D., of Franklin, died July 30. He was in his sixty-second year.

Dr. Richardson received his degree from Tufts College Medical School in 1907. He had been medical examiner of Norfolk County for twenty-one years. He was a fellow of the American Medical Association.

His widow, a son and a sister survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

POSTPONEMENT OF ELECTIVE TONSILLECTOMY

Inquiries are now being received by the Department of Public Health concerning the advisability of doing elective tonsillectomies during the summer months.

The present incidence of poliomyelitis is somewhat higher than that for the corresponding period of last year. Although this does not constitute the threat of a serious outbreak, the department is of the opinion that elective tonsillectomies should be postponed until the poliomyelitis season is over.

MISCELLANY

CHANGES IN ISOLATION AND QUARANTINE PROCEDURES FOR SCARLET FEVER

In line with modern thought on this common disease of childhood the Board of Health [City of New York] radically revised its isolation and quarantine procedures in scarlet fever on December 12, 1944. The regulations now include

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- 14 Study of postwar medical personnel requirements with special reference to the needs of the veterans' hospitals, the regular army, navy and United States Public Health Service.

story. We may hope that Dr. Champion's paper will prompt many readers to look for themselves to those earlier records reposing for years in the recesses of our libraries, too easily overlooked by "modern" medicine and "modern" public health. The fuller meanings of the closely linked sympathy of those two outstanding characters of our past century unfold gradually to the thoughtful reader after the manner of the theme of Osler's "The Growth of Truth."

One part of the Shattuck-Bowditch story, evidently important in the time when our first state health authority was taking form, stems from Shattuck's enthusiastic conviction that necessary agents of the "sanitary reform" he envisioned and advocated so zealously must be physicians of such knowledge and character, as were still rare attributes of the profession of his time. As part of the argument of his report to the legislature in 1850 for more adequate public measures in the prevention of disease witness this statement concerning duties of medical officers of health in Appendix XI of the 1850 Commission Report. "Preventive medicine while it constitutes a special [science] is in itself the highest and most useful branch of medicine and requires in its missionaries a correspondingly long and special study to become useful promulgators of its doctrines and workers in its cause." On one of the very early pages of this same report, witness also his reference to the famous question, "Who is the physician who is an honor to his profession?" And the immortal answer, in words attributed to Hippocrates himself: "He who has merited the esteem and confidence of the public by profound knowledge, long experience and consummate integrity, who has been led through all the circle of the sciences

The complement to Mr. Shattuck's high ideals of the unrealized social potentials of the medical profession is Dr. Bowditch's high esteem of Mr. Shattuck personally, of the public ideals that Shattuck represented and of his part in the getting the idea of preventive medicine officially recognized and accepted in the Commonwealth. Glimpses of this part of the picture appear in several accessible records. *The History of the Massachusetts Medical Society*, by Dr. W. L. Burrage, tells much and implies more. Dr. Bowditch himself commemorating the first century of medicine in the United States in an address before the National Medical Congress in Philadelphia in 1876, referred to Shattuck as one of two outstanding characters of the English-speaking world "prominent in their relation to the third epoch or that in which the medical profession is aided by the laity." In speaking further of Shattuck he said "There is no doubt that he, as a layman quietly working did more toward bringing Massachusetts to correct views on this subject than all other agencies whatsoever."

Pioneers of Public Health by M. E. M. Walker, contains a chapter on Shattuck along with those on Jenner, Pasteur, Lister and other such notables. This same manual refers also to that portion of Dr. Bowditch's centennial address of 1876 which reads as follows:

Twenty-five years ago viz. in 1850 a report of the Sanitary Commission of Massachusetts was printed by order of the Legislature. It was written chiefly, if not entirely, by a layman—Lemuel Shattuck, Esquire, an earnest sanitarian of that day. As I read it now after a lapse of a quarter of a century since it was written and presented to the Legislature I wonder at the wisdom of its suggestions and learn much from them. I remember Mr. Shattuck well—calm in his perfect confidence in the future of preventive medicine to check disease, he walked almost alone the streets of his native [adopted] city—not only unsustained by the profession but considered by most of them an offense of his candid advocacy of what seemed to the majority of physicians to be out of the layman's sphere and withal of trifling moment compared with our usual routine of so-called practice.

Thus in 1876, Dr. Bowditch one-time secretary of the Massachusetts Medical Society and one-time secretary of the American Medical Association chosen to review for assembled physicians of all nations the first century of medicine in the United States declared concerning the "third epoch" or that in which the medical profession had been aided by the laity, "The ruling idea of this epoch is still in its infancy but shows by what it has already accomplished trivial though this performance may seem at first glance to be its inherent

and great power, its objects are vastly wider than those of any preceding epoch." In that courageous declaration of young American medicine there appeared a vigorous new witness to the ancient truth that from time to time in the affairs of men, traditional antitheses unite in a new birth of freedom in procreative thought and action.

In the first annual report (1870) of the State Board of Health "to the honorable Senate and House of Representatives," Dr. Bowditch, as secretary, defined "the essential principles of action" of the new board and the place of physicians in carrying out those principles of action in these words:

By the careful and comprehensive study of these various laws [of health and life] and their relations the highest department of the physician's art is brought into operation, but no man or private body of men has the ability to study and develop this department as a free commonwealth can do when acting through the agency of a few persons who are devoted to this object and who come willingly to the work and armed with the power and ample means of the state.

In terms of individual life, seventy-five years means venerable maturity. In terms of growth of a social discipline, it usually means something quite different. The "ruling idea" of that epoch in which the medical profession was aided by the laity was only in its infancy when it imparted its drive to the developments that have become "seventy-five years of public health in Massachusetts" and that have lent their sanction to and determined the pattern of most of our subsequent public-health legislation.

What can this seventy-fifth anniversary report tell of the present "physical stature" and "mental age" of that promising infant idea, which Dr. Bowditch spoke of as the "ruling idea" of the new epoch? Today that same idea has rich possibilities that Shattuck and Bowditch could hardly have imagined. Compared with their time, this is a time of vastly amplified power and means, "professional" and "lay," within the society that is our commonwealth operating under the liberal principles of our social philosophy and of our chosen form of government. The stirring environment of this larger world, which sets new premiums on physical power and moral and spiritual stamina, also begins to define new objectives to give direction to this amplified power and means. Furthermore, against the background of the Shattuck-Bowditch time, we are a profession generously qualified to exercise our responsibilities in an enlarged "practice" in sincere fearless forward moving collaboration with the peoples who are today's "laity" through their agencies of government and other agencies of organized power and action.

The names of Pasteur and Lister have long stood for an epoch of the advance of medicine as a biologic science and art. Is it a too daring draft on our account with destiny to expect an equally distinguished maturity for the vigorous Shattuck-Bowditch conception of medicine as a social science and a growing social practice carrying the full benefits of medical knowledge to every family and every person in the Commonwealth? Of that idea which he considered then "the ruling idea—still in its infancy," Dr. Bowditch said in 1876 "Its early manhood will not be reached until far toward the termination of the next century."

Again we thank Merrill Champion for his timely contribution to the "child hygiene" of Massachusetts medicine.

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MIDDLESEX MEDICAL SOCIETY

To the Editor: In "The History of Middlesex North District Medical Society," which appeared in the July 12 issue of the *Journal*, Dr. Gardner states that the first medical association in Middlesex County was formed in 1829. Thacher's *American Medical Biography*, in its account of the Honorable Oliver Prescott, M.D., M.M.S. and A.A.S., states on page 429 of Volume I that he was "president of the Middlesex Medical Society during the whole period of its existence." Dr. Prescott was born in Groton in 1731 and died (of a pectoral dropsy) in 1804. What his "Middlesex Medical Society" amounted to

scarlet fever in the larger classification of "streptococcal sore throat, including scarlet fever," and change the isolation period in cases with no septic complications to the duration of the acute stage, the minimum period being seven days. The Board of Health further eliminated quarantine of household contacts to scarlet fever, making it no longer a requirement that such contacts stay out of school or work.

The action of the Board of Health was based on several factors. The first and most important of these is the fact that scarlet fever should not be considered a disease entity in itself, independent of other streptococcal throat infections. A large body of scientific work—clinical, bacteriological, immunological and epidemiological—indicates that the same hemolytic streptococcus (group A streptococci) which causes in one person septic sore throat, in another erysipelas and in a third puerperal sepsis may cause in a fourth the syndrome which for centuries has been known as scarlet fever. The type of clinical disease produced by infection depends on a number of factors—such as the previous history of streptococcal infection, the portal of entry of the infection and, to a certain extent, the characteristics of the particular strain of organism.

In many cases, the only distinction between septic sore throat and scarlet fever is the appearance of the rash, and there is ample evidence to indicate that the absence or presence of the rash is a phenomenon dependent on the individual's ability to withstand the so-called erythrogenic toxin of the hemolytic streptococcus. In other words, given two susceptible individuals exposed to the same hemolytic streptococcus, one person, because he is immune to the rash-producing mechanism, will have a sore throat without a rash, while the other person, nonimmune to this rash-producing toxin, will have scarlet fever. To have different regulations for persons suffering from the same disease, either with or without a rash, has for a considerable length of time been considered inconsistent.

The ineffectiveness of former quarantine measures was a second reason for the Board's decision. The age-old isolation measures, drastic as they were, had little or no effect on the incidence of streptococcal disease in general throughout the city. Moreover, from 1900 to the present there were different periods of isolation, yet there does not seem to be any close correlation between strict or liberal control of cases and the incidence of the disease. It seemed wiser, therefore, to put all streptococcal throat infections into one category with the same restrictive measures applying to all of them.

The majority of streptococcal throat infections, including scarlet fever, run their course in a week, and the hemolytic streptococcus responsible for the disease disappears in many cases or is reduced in numbers very considerably as soon as clinical recovery occurs. Since there are probably many more carriers of the hemolytic streptococci responsible for streptococcal throat infections including scarlet fever in the general population than in recovered cases, it was an undue hardship to require the strict isolation of convalescent streptococcal sore throat patients and scarlet fever convalescents until they were bacteriologically noninfectious, while allowing other carriers complete freedom of action.

The statement is occasionally made that complications of scarlet fever often do not set in until the second week, and that, consequently, cases should be isolated for at least two weeks. It is to be noted, therefore, that according to the Sanitary Code, cases of scarlet fever are isolated until recovery, but for a period of not less than one week. Complications following sore throat without a rash also frequently occur in the second week. Formerly such cases were not isolated.

A third reason for modifying the restrictions on scarlet fever was the experience which New York City shared with most of the United States and, in fact, with a great part of the world. Scarlet fever has become increasingly benign. It apparently reached a peak of severity during the last half of the nineteenth century and, since about 1875, has steadily become less severe. Available morbidity and mortality rates show a decrease in the case fatality rate of approximately 95 per cent from the earliest recorded rates to those of the present. This decline, however, has not been uniform, the northern states and urban areas showing more marked decreases than the southern states and rural areas. There seems to be no obvious explanation of this trend, but in the United States at the present time, there is no doubt that we are in a very mild phase of the cycle of the disease.

deaths from scarlet fever in New York City are becoming very infrequent and the disease itself from the clinical standpoint certainly is a much milder one than is ordinarily associated with the word scarlet fever.

It was only after very careful consideration of the entire situation that the Board of Health, in line with the scientific evidence adduced above, modified the New York City regulations regarding scarlet fever. The New York State Department of Health, through its Public Health Council, adopted similar regulations.—Reprinted from *Quarterly Bulletin, Department of Health, City of New York, July, 1945*

* * *

The above article explains, in more or less detail, the reasons for changes recently made by the New York City Department of Health regarding the isolation of patients with scarlet fever. These regulations were commented on editorially in the May 10 issue of the *Journal*.—Ed

CORRESPONDENCE

THE SUFFIX "-OSIS"

To the Editor Having been educated at the feet of those Harvard scholars who challenge the world with their pronunciation of such words as "vertebral," "trachea" and "appendicitis," I have also developed somewhere along the line an acquired (or—shades of my Salem ancestors—could it be an atopic?) sensitivity to words ending in "-osis." Consequently I read with particular interest both the title and the substance of the article "Death from Sulfadiazine with Agranulocytosis, Jaundice and Hepatosis" by Ziegler et al. in the July 19 issue of the *Journal*.

Perhaps my Gould's dictionary is obsolete, but it does not give a definition of hepatosis. It does list "nephrosis (any renal disease)" and "polypsis (the condition of being afflicted with polyps)." What I should like to know is, is a person with hepatosis afflicted with livers or does he just have any old hepatic disease?

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* * *

The *Journal* has often been criticized for its use of "-ic" and "-ical," but this is the first time that "-osis" has been so honored. According to Dorland's *American Illustrated Medical Dictionary* (twentieth edition), nephrosis means "any functional disorder of the liver." Since autopsy in the case referred to by Dr. Edsall failed to show a definite pathologic lesion, the word in question appears to be the proper one to have used.—Ed

SHATTUCK AND BOWDITCH

To the Editor The leading article in the March 1, 1945 issue of the *Journal*, "Seventy-Five Years of Public Health in Massachusetts," is a timely reminder of one of those momentous conjunctions of individualities which, from time to time, have lighted new beacons and reset the course of progress.

Somewhat earlier, the names of Edwin Chadwick and Dr. John Simon had become associated in the English language of public health. About the same time, the names of Pasteur and Lister were coming to stand for new ideas in the science and the practice of surgery and medicine.

We all may be grateful to Merrill Champion for his terse restatement of long-recorded facts which made the Shattuck-Bowditch phenomenon of our own commonwealth one of those luminous combinations of personalities and ideas that is still a herald of light to illumine the present status of Massachusetts medicine and to project at least one ray beyond our present day.

Dr. Champion's account of Lemuel Shattuck as "pioneer" and Dr. Henry I. Bowditch as "organizer" is a well balanced sketch of outstanding events of the period 1849 to 1879, in which have proved so full of meaning for public health in the Commonwealth and beyond our boundaries. Naturally, the pages of such an article cannot reproduce the complete

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LIGATION OF THE INFERIOR VENA CAVA FOR THE PREVENTION OF PULMONARY EMBOLISM*

A Report of Two Cases

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THROMBOSIS in the deep veins of the lower extremities has been shown to be a frequent source of postoperative pulmonary emboli. The demonstration by Homans,¹⁻³ Frykholm⁴ and others that such thromboses usually begin in the veins of the foot or lower leg, with later extension into the femoral and iliac veins, has led to enthusiastic attempts to prevent embolic sequelae by venous ligation proximal to the thrombotic process. Because of their easy accessibility and the fact that in early cases they lie above the site of thrombosis, the superficial and common femoral veins have generally been chosen as the sites of ligation.

The results of femoral-vein ligation have been encouraging not only for the prevention of pulmonary embolism but as a means of preventing the chronic, disabling symptoms that otherwise result. In a small percentage of cases, from the development of a full-fledged phlegmasia alba dolens. In 1941, Sears⁵ reported 10 cases of femoral-vein ligation with no untoward results. In 1943, Allen, Linton and Donaldson⁶ reported ligations in 202 patients, in 78 cases bilateral ligation was done. The postoperative sequelae in this series were surprisingly few, edema of the legs being the most serious. The average patient wore an elastic bandage for a period of only three or four weeks before regarding it as unnecessary. It was also found that early swelling of the legs was slightly more frequent following interruption of the common femoral vein, whereas late edema was about equally frequent following ligation of the superficial or common vein.

Homans⁷ has recently suggested that when a partially obstructing thrombus is found at or above the level of the common femoral vein, ligation of the common iliac vein gives greater protection against

embolism than does removal of the thrombus and ligation of the common femoral vein. He points out that ligation of the common iliac vein also allows a more satisfactory collateral pathway for venous return around the point of ligation. This collateral pathway extends upward through the deep circumflex iliac and deep epigastric veins. Of more importance are the internal iliac (hypogastric) veins, whose numerous anastomoses with each other allow the blood to be shunted across the pelvis to the iliac vessels of the side opposite the ligation. In a series of 14 common iliac interruptions no postoperative edema was noted.

The advantages of common iliac vein ligation are to a certain extent outweighed by the more extensive operative procedure that is required to isolate this vessel. Homans has used an extraperitoneal approach that is satisfactory only for unilateral ligation. He states that ligation of the inferior vena cava is probably indicated in the presence of bilateral thrombosis and is certainly to be preferred to bilateral common iliac vein ligation. The experience of Allen, Linton and Donaldson⁶ in regard to bilateral thrombosis is of interest in this connection. They state, "We have found thrombosis in so many supposedly normal extremities that we are inclined to feel that simultaneous routine interruption of the opposite [femoral] vein should be undertaken." If it is true that venous thrombosis is a disease that frequently affects the vessels of both lower extremities and if, in advanced cases of femoroiliac thrombosis, it is true, as it almost certainly is, that ligation above the site of thrombus formation gives added protection against embolism, ligation of the inferior vena cava seems desirable, first to interrupt the venous channel above the evident femoroiliac thrombosis, and second to prevent embolism from a simultaneous, subclinical phlebothrombosis that is probably frequently present in the veins of the opposite lower leg.

Although it seems evident that, in the great ma-

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and how long it lasted I do not know, but it probably was organized in the eighteenth century

This letter intends to supplement rather than challenge Dr Gardner's excellent paper, and it perhaps may call forth other fragments concerning early medical days in Middlesex County

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DWIGHT O'HARA

MEDICAL SCHOOLS AND COMPULSORY MEDICAL INSURANCE

To the Editor This is a note on a possible solution of the question as to the position of medical schools under compulsory medical insurance

This year the Governor of California introduced a compulsory health insurance bill (A B 800). The Congress of Industrial Organizations, which had long been studying health insurance, introduced another bill (A B 449) that differed from the Governor's on several important details

The Governor's bill made no reference to medical schools. After the Governor, however, had consulted with the deans of the four schools in the State he announced that if the schools should happen to treat beneficiaries under the act they would not ask that more than their expenses be covered and that so far as teaching was concerned "medical indigents" would still be available

Under the CIO bill, indigents received benefits and the number of those covered by the provisions of service was so large that the point was raised that most of the people who are now coming to the medical schools might go to private doctors. The authors of the CIO bill recognized the seriousness of this possibility in regard to medical teaching. They looked on medical schools as the organizations best equipped to forward that maintenance and improvement of the quality of medical care without which a mere extension in quantity might prove a dubious blessing. Therefore, the bill provided that representatives of medical schools be appointed on both the central and local governing bodies under the act. To make sure that these representatives should be in close touch with advancing knowledge it was required that they should be selected from those who were in whole-time investigation and teaching. To avoid the danger of bureaucratic or political interference it was provided that medical schools, or any other group capable of giving complete and adequate medical service, might be paid a lump sum for all they did, leaving them free to spend the money in any way they desired. Universities might thus give some of it to research work and some of it to younger men who now work for nothing. The indications were that the amount of money that would be thus put at the disposal of the universities might be so large that the present crippling of medical-school work from lack of money would largely disappear. With practice passing more and more into the hands of a series of interconnected groups of doctors, working in rural areas around medical centers, in district towns around hospitals and coming to an apex in medical schools, it was felt that people would be eager to be treated by medical-school groups and that the great majority would welcome a discussion of their medical problems with medical students

The reaction of medical students to these proposals in the CIO bill was interesting. At the University of California Medical School, 106 students signed a petition to their dean in which the advantages of the plan for all medical schools were stressed. At Stanford, 209 students, practically the entire student body who could be reached in the time available, sent a petition to the Dean, the President, the Board of Trustees and the Alumni Association urging them to work for the adoption of the medical-school provisions of the bill. This substantial unanimity was achieved because the question of the advisability of compulsory medical insurance was not raised. The point that they were making was that if compulsory insurance became law they wanted their medical schools to take an active part in maintaining and advancing the quality of the care given to the people, to accept from the government the money due to the schools for the services they rendered and to maintain their freedom by keeping the disposal of the money received in the hands of the universities

Although this bill was killed in committee, the question of the status of medical schools under compulsory medical in-

surance will be raised again, and so the plan that was proposed is still important as the first constructive solution of a difficult problem that has found expression in concrete legislative form

T ADDIS

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BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request

The Woman Asks the Doctor By Emil Novak, M.D., associate in gynecology, Johns Hopkins University School of Medicine, and gynecologist, Bon Secours and St. Agnes hospitals. 8°, cloth, 130 pp., with 11 illustrations. Second edition. Baltimore: Williams and Wilkins Company, 1944. \$1.50

Much new material has been added to this second edition of a popular work on menstruation and its disorders. The author, who is an eminent gynecologist, discusses only those problems in which all women are interested and those in which he believes they most need instruction. This manual is recommended for collections on popular medicine.

NOTICES

ANNOUNCEMENT

Dr Bennett Solomon announces the reopening of his office at 145 State Street, Springfield 3

AMERICAN BOARD OF OPHTHALMOLOGY

The American Board of Ophthalmology announces the following examinations in 1946: Chicago, January 18 to 22 inclusive; Los Angeles, January 28 to February 1 inclusive; New York City, May or June; and Chicago, October. Owing to transportation difficulties the examination, originally scheduled for October 1945 in Chicago, has been postponed

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, AUGUST 23

FRIDAY AUGUST 24

*9:00-10:00 a.m. Medical clinic Isolation Amphitheater Children's Hospital
10:50 a.m. Bacterial Infections of the Skin Dr. George Morris (Postgraduate clinic in dermatology and syphilology) Amphitheater, Mallory Building Boston City Hospital

MONDAY AUGUST 27

*12:00 m-1:00 p.m. Clinicopathological conference Peter Best Brigham Hospital

TUESDAY AUGUST 28

*9:00-10:00 a.m. Medical clinic Infants Hospital
*12:15-1:15 p.m. Clinicorontogenological conference Peter Best Brigham Hospital

WEDNESDAY AUGUST 29

*12:00 m Clinicopathological conference Children's Hospital

*Open to the medical profession

SEPTEMBER 13 The Hemorrhagic Diseases Dr. William Dameshek
Pentucket Association of Physicians 8:30 p.m. Haverhill

SEPTEMBER 37 American Public Health Association Page 572, issue of November 30

OCTOBER 1-6 Medicolegal conference and seminar Page 776 Issue of June 28

ated with gauze strips saturated with boric acid ointment and held in place with firm elastic bandages. On this regimen evidence of sepsis disappeared and rapid epithelialization on both the periphery and numerous small epithelial "islands" occurred. On the 22nd day, the patient was allowed out of bed, and during the next 4 days she was permitted progressively increasing activity.

On the 27th day, the patient first complained of pain in the right chest posteriorly. This pain was associated with a rise in temperature to 102°F and sudden elevation of the respiratory rate to 38. Auscultation of the chest showed no evidence of consolidation, but coarse, moist rales were heard at the base of the right lung posteriorly. An x-ray film of the chest showed a small area of increased density. The legs were carefully examined. The burned areas were free of sepsis and completely epithelialized except for a few small areas, approximately 1 cm in diameter, which were covered with healthy granulation tissue. There was no evidence of deep superficial phlebitis in either leg. The dorsalis pedis and posterior tibial arteries showed good pulsation. The legs were warm, with no evidence of peripheral vasoconstriction, there was no dilatation of the veins or evidence of edema. Homans's sign was negative, and no tenderness was elicited over the femoral veins or the calves.

In the belief that the patient had an asymptomatic phlebotrombosis, probably arising in the veins of the lower extremities, operation was immediately performed under local anesthesia. Because the burned areas extended over the lower thirds of the thighs, areas drained by the deep femoral veins, the common femoral vein on each leg was isolated, doubly ligated and divided. Before ligation each vein was opened between traction ligatures. No evidence of clot was found, and there was a free flow of blood from both the proximal and distal segments.

Following bifemoral ligation the chest pain promptly disappeared and, within the first 24 hours, the pulse and respiratory rates fell to normal. Bicycle exercises were started immediately after operation, and on the 3rd postoperative day the patient was allowed out of bed. In spite of the improvement in her general condition, however, the temperature continued to fluctuate between 99 and 101°F. Three days after the femoral ligations the rales at the right base had disappeared. On this day the patient complained of slight pain over the lower chest anteriorly, which lasted only a few minutes and was not associated with an increase in respiratory rate. An x-ray film of the chest taken on the following day showed no change in the area of increased density previously noted at the base of the right lung.

Eight days after the bifemoral ligation the patient was awakened by the sudden onset of severe pain in the mid-clavicular region, associated with an elevation of the pulse and respiratory rate. A third x-ray film of the chest showed no change in the area at the right base, the left lung remaining clear. An electrocardiograph showed inversion of T₂ with slight right-axis deviation. The patient appeared acutely ill, there was slight cyanosis of the lips and fingernails, and her respirations were deep and labored. She was immediately placed in an oxygen tent, with some improvement in color. Intravenous fluids were administered, and 8 hours later her condition had improved sufficiently so that ligation of the inferior vena cava was undertaken, since it seemed evident that she had suffered a major pulmonary infarction.

Ligation of the inferior vena cava was done under spinal anesthesia through a long right paramedian incision in the center of which was at the level of the umbilicus. With the patient in the Trendelenburg position, the intestine was displaced into the upper abdomen and the posterior parietal peritoneum was incised to the right of the midline over the inferior vena cava. The cava was freed from the aorta without difficulty and doubly ligated with nylon ties, at the level of the bifurcation of the aorta. The duodenum and right ureter were identified and care was taken to avoid injury to them.

During the operation the blood pressure fell to 90/60, but responded promptly to the administration of intravenous glucose solution. At the end of the operation, which required 75 minutes, the blood pressure was 130/85. The pulse reached a maximum of 100 during the operation. When the patient was transferred to bed, however, it promptly rose to 150, but during the next 2 hours fell to 130, where it remained for the following 48 hours. The continued elevation of the pulse during this period was a matter of some concern, since it was

feared that, owing to the accumulating edema fluid in the legs, it might be an indication of incipient shock. The pulse, however, did not respond to the administration of intravenous fluids consisting of glucose in distilled water, whole blood and plasma. Because the respirations continued to be somewhat labored and slight cyanosis persisted, the patient was placed in an oxygen tent on the 2nd postoperative day. Shortly thereafter the pulse fell to 100. The rapid pulse was therefore believed to be due to diminished vital capacity resulting from the pulmonary infarct.

The circulation of the lower extremities was followed closely. Immediately following operation the skin of the feet, legs and thighs was mottled and cyanotic. This persisted for only a few hours. The arterial pulsations of both feet remained good. The legs were kept elevated on pillows and, at the end of 24 hours, only the slightest amount of pitting edema could be found around the ankles. This had increased slightly at the end of 48 hours. Thereafter both legs were securely bound with elastic bandages from the toes to the groins and further edema did not accumulate while the patient remained in bed.

During the first 2 postoperative days there was profuse sweating, and this, together with mild edema of the lower extremities, caused the urinary output to be low in spite of adequate amounts of intravenous fluids. At the end of this interval the blood nonprotein nitrogen had risen to 58 mg per 100 cc. The total serum protein was 8 gm per 100 cc. On the 3rd postoperative day the sweating became less and the urinary output increased, but the nonprotein nitrogen did not fall to normal until the 6th postoperative day.

After the first 48 hours the patient's general condition progressively improved. The wound healed by first intention. Bicycle exercises were started on the 3rd postoperative day and were continued several times daily thereafter. She was allowed out of bed on the 12th day, with the legs and thighs tightly swathed in elastic bandages. Only slight pitting edema of the lower thirds of the legs and of the ankles occurred when she became ambulatory. She was discharged from the hospital in good condition on the 18th postoperative day. Before discharge an effort was made to secure a phlebogram to demonstrate the collateral circulation around the ligated common femoral veins and around the caval ligation. These efforts were unsuccessful because the small size of the veins would not permit sufficiently rapid introduction of the dye. The small foot veins also made it impossible to secure satisfactory venous pressure readings.

Two months after the operation the patient's only complaint was of pitting edema of both lower legs. At that time enlarged veins extended from the groins upward along the lateral aspects of the abdomen and chest to the axillae. Four months after operation these veins had entirely disappeared, there was no evidence of peripheral edema, and the patient was allowed to return to light work.

CASE 2 A 71-year-old man was admitted on August 17, 1944, complaining of painful swelling of the left foot of 1 week's duration. Nine months previously he had noted a draining sinus on the medial aspect of the first metatarsophalangeal joint, which had persisted for 1 week. Thereafter he remained well until 1 week before admission, when pain, tenderness and local swelling recurred. Three days later a slight purulent discharge was noted. During the 4 days preceding admission the pain, swelling and tenderness became progressively worse and he was referred to the hospital by his physician.

Thirty-five years previously the patient was told that he had heart disease. His only symptom was mild dyspnea on exertion. Fifteen years later, cholecystectomy and appendectomy were done. Otherwise the past history was non-contributory.

Physical examination revealed a well developed and well nourished man who appeared to be acutely ill. The temperature was 101.6°F, the pulse 90, and the respirations 24. The head and neck showed no abnormalities. Excursions of the chest were equal but limited on both sides. The lung fields were resonant, with vesicular breathing throughout. Scattered, fine, moist rales were heard at the bases of both lungs. The heart was slightly enlarged, the left border of dullness being 2 cm outside the midclavicular line. A soft systolic murmur was heard at the apex. The blood pressure was 180/100. The abdomen showed a well healed scar over the right upper rectus muscle but was otherwise normal. The

majority of cases, pulmonary embolism arises from venous thromboses that originate in the veins of the lower leg and later progress upward to involve the pelvic veins, there are some cases in which the thrombotic process arises in the pelvic veins themselves. Rössle⁸ found from post-mortem studies that the hypogastric and iliac veins were involved in the thromboembolic process without involvement of the veins of the calf in only about 10 per cent of cases. Bauer,^{9, 10} however, concluded from venographic studies that almost invariably the thromboembolic process starts in the deep, large venous trunks of the lower leg.

Henderson,¹¹ reporting on 313 cases of fatal pulmonary embolism among surgical cases that came to autopsy, found the origin of the emboli in 189 cases to be as shown in Table 1. In some of the

TABLE 1 Source of Emboli in 189 Fatal Cases (Henderson¹¹)

Source	No.
Iliac vein	64
Femoral vein	53
Pelvic veins	43
Prostatic plexus	18
Vena cava	13
Hemorrhoidal veins	1
Vaginal plexus	1
Cervical plexus	1
Right auricle	10
Renal vein	7
Axillary vein	3
Right ventricle	3
Ovarian veins	3
Deep epigastric vein	1
Jugular vein	1
Subclavian vein	1
Azygos vein	1
Innominate vein	1
	31
Total	227

cases two or even three sites of thrombosis were found. It is to be noted that in this series of 227 veins involved by thrombosis, 196 (86 per cent) were direct or indirect tributaries of the lower third of the inferior vena cava.

Numerous reports of experimental rapid occlusion of the inferior vena cava by ligation have been published, beginning with the work of Lower¹² in 1669. It has been repeatedly and conclusively shown that ligation above the level of the renal veins results in death, usually with an accompanying anuria and uremia. Below the level of the renal veins experimental ligation of the inferior vena cava is compatible with life, carries a low mortality rate and is associated with only slight and transient edema of the lower extremities.

Ligation of the inferior vena cava in man has been reported with increasing frequency. Pleasants¹³ in 1911, in a fairly complete review of the literature, found reports of 8 cases in which surgical ligation of the inferior cava had been performed. In all these cases ligation was done in connection with operations on the kidney. Ochsner and DeBakey¹⁴ in 1941 commented on a series of 48 cases of caval ligation, collected by Krotoski, chiefly performed for septic thrombophlebitis resulting from puerperal infection.

Collins, Jones and Nelson^{15, 16} in 1943 reported series of 41 cases of pelvic thrombophlebitis proved at operation or at autopsy. Pulmonary embolism was found in 85 per cent. In 8 cases ligation of the inferior vena cava was done, with 1 death, a mortality of 13 per cent.

From the above considerations it seems evident that ligation of the inferior vena cava below the level of the renal veins, although an operation of considerable magnitude, is compatible with survival in both experimental animals and man. A consideration of the available collateral pathways for venous return around the point of ligation^{7, 12} indicates that an eventual return to normal venous pressure relations should ensue. That this is true, as shown clinically by the gradual disappearance of post-operative edema, is evidenced by the end results of the cases presented below.

The indications for ligation of the inferior vena cava are not well defined. The following cases are presented to illustrate two situations in which such an operation has been followed by recovery. In each case the caval interruption probably forestalled a fatal issue by preventing massive pulmonary embolism. At the time of caval ligation both had suffered multiple pulmonary infarcts. From the standpoint of the peripheral venous system the indications for caval interruption were thrombosis arising in and confined to the veins of the pelvis, and iliac thrombosis arising by propagation from the vessels of the leg and associated with possible or probable thrombosis in the veins of the opposite leg.

CASE REPORTS

CASE 1. A 49-year-old, married woman was admitted to the Framingham Union Hospital on July 8, 1944, complaining of burns of the inner aspect of both thighs. The past history was significant in that 24 years previously, following the birth of the first child, the veins of the right lower leg became prominent and painful. The patient could recall no swelling of the leg, although her obstetrician told her that she had phlebitis. The post-partum course was otherwise normal. Since this episode occasional prominence of superficial veins below the right patella associated with a "drawing sensation" had been noted, although there had never been any edema of the leg or ankle.

Shortly before admission to the hospital, a pot of coffee was dropped and the patient received burns of the anteromedial aspects of both thighs just above the knees. Examination revealed a well developed, somewhat obese woman who appeared to be in good health. The general physical examination disclosed nothing of note. The heart and lungs were normal, and the blood pressure was 147/90. On the anteromedial aspect of both thighs, just above the knees, were areas of vesication from the burns, each 15 cm in diameter. No abnormalities of the peripheral circulation were noted in either of the lower extremities. Each of the burned areas was debrided and sprayed with 1 per cent aqueous gentian violet until a firm eschar had formed.

Laboratory examination showed the urine to be acid with a specific gravity of 1.025 and to contain 30 mg per 100 cc of albumin. There was no sugar. The sediment showed no cells but innumerable bacteria. The red-cell count was 4,850,000 and the hemoglobin 15.5 gm. The white-cell count was 6400, with a normal differential count.

Except for a low-grade fever caused by mild infection of the burned areas, and easily controlled by removal of the gentian eschar, the first 2 weeks of hospitalization were without incident. During the 3rd week the burned areas were

ted with gauze strips saturated with boric acid ointment held in place with firm elastic bandages. On this regimen evidence of sepsis disappeared and rapid epithelialization on both the periphery and numerous small epithelial "islands" occurred. On the 22nd day, the patient was allowed out of bed, and during the next 4 days she was permitted progressively increasing activity.

On the 27th day, the patient first complained of pain in the chest posteriorly. This pain was associated with a rise in temperature to 102°F and sudden elevation of the respiratory rate to 38. Auscultation of the chest showed no evidence of consolidation, but coarse, moist rales were heard at the base of the right lung posteriorly. An x-ray film of the chest showed a small area of increased density. The legs were carefully examined. The burned areas were free of sepsis and completely epithelialized except for a few small areas, approximately 1 cm in diameter, which were covered with healthy granulation tissue. There was no evidence of deep superficial phlebitis in either leg. The dorsalis pedis and anterior tibial arteries showed good pulsation. The legs were warm, with no evidence of peripheral vasoconstriction, there was no dilatation of the veins or evidence of edema. Homans' sign was negative, and no tenderness was elicited over the popliteal veins or the calves.

In the belief that the patient had an asymptomatic phlebotrombosis, probably arising in the veins of the lower extremities, operation was immediately performed under local anesthesia. Because the burned areas extended over the lower thirds of the thighs, areas drained by the deep femoral veins, a common femoral vein on each leg was isolated, doubly ligated and divided. Before ligation each vein was opened between traction ligatures. No evidence of clot was found, and there was a free flow of blood from both the proximal and distal segments.

Following bifemoral ligation the chest pain promptly disappeared and, within the first 24 hours, the pulse and respiratory rates fell to normal. Bicycle exercises were started immediately after operation, and on the 3rd postoperative day the patient was allowed out of bed. In spite of the improvement in her general condition, however, the temperature continued to fluctuate between 99 and 101°F. Three days after the femoral ligations the rales at the right base had disappeared. On this day the patient complained of slight pain over the lower chest anteriorly, which lasted only a few minutes and was not associated with an increase in respiratory rate. An x-ray film of the chest taken on the following day showed no change in the area of increased density previously noted at the base of the right lung.

Eight days after the bifemoral ligation the patient was awakened by the sudden onset of severe pain in the mid-apical region, associated with an elevation of the pulse and respiratory rate. A third x-ray film of the chest showed no change in the area at the right base, the left lung remaining clear. An electrocardiograph showed inversion of T₁ with slight right-axis deviation. The patient appeared acutely ill, there was slight cyanosis of the lips and fingernails, and the respirations were deep and labored. She was immediately placed in an oxygen tent, with some improvement in color. Intravenous fluids were administered, and 8 hours later her condition had improved sufficiently so that ligation of the inferior vena cava was undertaken, since it seemed evident that she had suffered a major pulmonary infarction.

Ligation of the inferior vena cava was done under spinal anesthesia through a long right paramedian incision, the center of which was at the level of the umbilicus. With the patient in the Trendelenburg position, the intestine was displaced into the upper abdomen and the posterior parietal peritoneum was incised to the right of the midline over the inferior vena cava. The cava was freed from the aorta without difficulty and doubly ligated with nylon ties, at the level of the bifurcation of the aorta. The duodenum and right ureter were identified and care was taken to avoid injury to them.

During the operation the blood pressure fell to 90/60, but responded promptly to the administration of intravenous glucose solution. At the end of the operation, which required 5 minutes, the blood pressure was 150/85. The pulse reached a maximum of 100 during the operation. When the patient was transferred to bed, however, it promptly rose to 150, but during the next 2 hours fell to 130, where it remained for the following 48 hours. The continued elevation of the pulse during this period was a matter of some concern, since it was

feared that, owing to the accumulating edema fluid in the legs, it might be an indication of incipient shock. The pulse, however, did not respond to the administration of intravenous fluids consisting of glucose in distilled water, whole blood and plasma. Because the respirations continued to be somewhat labored and slight cyanosis persisted, the patient was placed in an oxygen tent on the 2nd postoperative day. Shortly thereafter the pulse fell to 100. The rapid pulse was therefore believed to be due to diminished vital capacity resulting from the pulmonary infarct.

The circulation of the lower extremities was followed closely. Immediately following operation the skin of the feet, legs and thighs was mottled and cyanotic. This persisted for only a few hours. The arterial pulsations of both feet remained good. The legs were kept elevated on pillows and, at the end of 24 hours, only the slightest amount of pitting edema could be found around the ankles. This had increased slightly at the end of 48 hours. Thereafter both legs were securely bound with elastic bandages from the toes to the groins and further edema did not accumulate while the patient remained in bed.

During the first 2 postoperative days there was profuse sweating, and this, together with mild edema of the lower extremities, caused the urinary output to be low in spite of adequate amounts of intravenous fluids. At the end of this interval the blood nonprotein nitrogen had risen to 58 mg per 100 cc. The total serum protein was 8 gm per 100 cc. On the 3rd postoperative day the sweating became less and the urinary output increased, but the nonprotein nitrogen did not fall to normal until the 6th postoperative day.

After the first 48 hours the patient's general condition progressively improved. The wound healed by first intention. Bicycle exercises were started on the 3rd postoperative day and were continued several times daily thereafter. She was allowed out of bed on the 12th day, with the legs and thighs tightly swathed in elastic bandages. Only slight pitting edema of the lower thirds of the legs and of the ankles occurred when she became ambulatory. She was discharged from the hospital in good condition on the 18th postoperative day. Before discharge an effort was made to secure a phlebogram to demonstrate the collateral circulation around the ligated common femoral veins and around the caval ligation. These efforts were unsuccessful because the small size of the veins would not permit sufficiently rapid introduction of the dye. The small foot veins also made it impossible to secure satisfactory venous pressure readings.

Two months after the operation the patient's only complaint was of pitting edema of both lower legs. At that time enlarged veins extended from the groins upward along the lateral aspects of the abdomen and chest to the axillae. Four months after operation these veins had entirely disappeared, there was no evidence of peripheral edema, and the patient was allowed to return to light work.

CASE 2 A 71-year-old man was admitted on August 17, 1944, complaining of painful swelling of the left foot of 1 week's duration. Nine months previously he had noted a draining sinus on the medial aspect of the first metatarsophalangeal joint, which had persisted for 1 week. Thereafter he remained well until 1 week before admission, when pain, tenderness and local swelling recurred. Three days later a slight purulent discharge was noted. During the 4 days preceding admission the pain, swelling and tenderness became progressively worse and he was referred to the hospital by his physician.

Thirty-five years previously the patient was told that he had heart disease. His only symptom was mild dyspnea on exertion. Fifteen years later, cholecystectomy and appendectomy were done. Otherwise the past history was non-contributory.

Physical examination revealed a well developed and well nourished man who appeared to be acutely ill. The temperature was 101.6°F, the pulse 90, and the respirations 24. The head and neck showed no abnormalities. Excursions of the chest were equal but limited on both sides. The lung fields were resonant, with vesicular breathing throughout. Scattered, fine, moist rales were heard at the bases of both lungs. The heart was slightly enlarged, the left border of dullness being 2 cm outside the midclavicular line. A soft systolic murmur was heard at the apex. The blood pressure was 180/100. The abdomen showed a well healed scar over the right upper rectus muscle but was otherwise normal. The

prostate was small, of normal consistence and nontender. The right foot showed no abnormalities, and the arterial pulsations were normal. On the medial surface of the first metatarsophalangeal joint of the left foot was the opening of a sinus from which a small amount of thin, odorless pus drained. A smear of this material showed the presence of a staphylococcus that was later identified as *Staphylococcus albus*. From the opening of this sinus an area of cellulitis extended over the dorsum of the foot to the level of the malleoli. This area was red, hot and moderately tender. No evidence of lymphangitis was present, although inflammatory edema extended up to the knee. Arterial pulsations could not be identified, although there was a good inflammatory reaction, and the non-inflamed areas were warm, indicating a satisfactory collateral circulation. No enlarged inguinal nodes were palpable.

The specific gravity of the urine varied from 1.010 to 1.022. On admission no albumin was found, but in subsequent specimens it varied from 100 to 190 mg per 100 cc. No sugar was found in the urine in routine or premeal specimens, although the fasting blood sugar was 153 mg per 100 cc. The urine sediment contained no cells at the time of admission, but subsequently as many as 90 to 100 white cells were found per high-power field. The red-cell count was 3,800,000, and the hemoglobin 14.5 gm. The white-cell count was 11,700 with 89 per cent neutrophils. The nonprotein nitrogen was 53 mg per 100 cc on admission, subsequently falling to 28 mg. The total serum protein was 7.3 gm per 100 cc with 5.0 gm of albumin and 2.3 gm of globulin, a ratio of 2:1. The whole blood chloride was 493 mg per 100 cc, expressed as sodium chloride.

X-ray examination of the foot showed calcification in the blood vessels. There was marked decalcification of the bones, but no evidence of osteomyelitis.

Immediately after admission sulfadiazine was begun and the patient received a total of 4 gm. On the evening of the 1st day, however, he suffered a severe chill, followed by a temperature of 104.8°F. Because of the elevated nonprotein nitrogen, sulfadiazine was discontinued and penicillin was begun in doses of 20,000 Oxford units intramuscularly every 4 hours. The inflammation was treated locally with elevation and constant, wet heat. On this regimen the infection localized, and 4 days later incision and drainage was done under local anesthesia. Following drainage the temperature promptly fell to normal, where it remained for 3 days.

On the evening of the 3rd postoperative day, a sudden increase of respirations to 24 was noted and the pulse rose from 80 to 96. The patient complained of lower-abdominal pain. Examination revealed a distended bladder that on catheterization yielded 2220 cc of urine. Until that time the patient had been voiding in large amounts and had had a satisfactory total daily output. Following catheterization the abdominal pain was relieved but the respirations remained elevated. In retrospect it seems likely that the first pulmonary embolus occurred at that time and was followed by acute urinary retention. Repeated examinations of the chest during the following 6 hours showed nothing of diagnostic importance. The legs were carefully examined and showed no tenderness of the calves or thighs. Homans's sign was negative on the right leg but could not be obtained on the left side because of the draining wound over the left ankle.

On the following day the temperature rose to 102.4°F, and during the following 4 days it fluctuated around 101°F. An x-ray film of the chest taken on the day of the first temperature rise showed the lung fields to be clear. The aorta was tortuous and showed some calcification in its arch. The left ventricle was prominent. The chest film was repeated 3 days later and again showed the lung fields to be clear.

Although a pulmonary embolus was strongly suspected and the legs were examined several times daily, it was not until the fifth day after the onset of chest symptoms that tenderness could be elicited in the left calf and over the course of the left femoral vein in the thigh. At that time slight induration was found over the course of the vein, suggesting that the femoral vein, as well as the iliac vein, was solidly thrombosed. Because of the continued fever, associated with an irregular elevation of the respiratory rate, it was believed that the patient had suffered multiple small pulmonary emboli, none of sufficient size to cause a visible change on the x-ray plate.

The patient was immediately transported to the operating room, where the left femoral vein was exposed under local anesthesia. The common femoral vein was opened between

traction ligatures and found to contain an adherent thrombus that completely occluded its lumen. With a large suction tip an effort was made to remove this clot from the common femoral and external iliac veins. A rather large amount was removed, but only a trickle of blood was obtained from the proximal segment, indicating that it extended well into the common iliac vein. The common femoral vein was doubly ligated and divided and the wound closed. In the portion of the femoral vein from which the thrombus was removed it was noted that the intima was destroyed in many small areas so that tiny bits of clot remained adherent, giving it a irregular, patchy appearance. The impression was gained that, had the thrombus been completely removed and a good flow of blood obtained from the proximal segment, the patchy destruction of the intima would have allowed the clot to re-form in the part of the vein proximal to the ligation. The danger of embolism would therefore probably not have been reduced by femoral ligation.

A decision was made to ligate the inferior vena cava. Under spinal anesthesia, supplemented with intravenous Pentothal Sodium, a long right-rectus-splitting incision was made, with its center at the level of the iliac crest. The patient was placed in the Trendelenburg position and the intestine was displaced into the upper abdomen. The posterior parietal peritoneum was incised over the inferior vena cava. There was a considerable amount of fat in this region, and it was with some difficulty that the cava was isolated from the aorta. The duodenum and right ureter were visualized and carefully avoided. A No. 6 nylon ligature was passed around the vena cava at the level of the bifurcation of the aorta. Preoperatively it was intended that the cava should be opened and searched for clot, since clot extending up the inferior vena cava for a distance 12 to 15 cm. has been found,⁷ but shortly before the ligature was applied the patient became restless and cyanotic and it was thought wise to terminate the operation as rapidly as possible. The cava was therefore ligated twice, in continuity, the ligatures being about 1 cm. apart, and the vessel was not opened. No change in pulse or blood pressure was noted at the time the caval lumen was obliterated. The posterior peritoneum was closed with a catgut suture, the intestines replaced, and the abdominal wall repaired. At the beginning of the operation the pulse was 94 and the blood pressure 140/80. At its termination 65 minutes later the pulse was 80 and the blood pressure 85/44. Following operation, elastic bandages were applied to the legs and thighs, the lower extremities were elevated and the patient was placed in an oxygen tent and was given 500 cc of plasma followed by 500 cc of 5 per cent glucose in distilled water intravenously. Immediately following operation profuse perspiration was noted, the extremities were cold, and the patient appeared to be in mild shock. The pulse, however, remained slow, and following the intravenous plasma and glucose the blood pressure returned to 120/85. The profuse perspiration continued for 36 hours, well after other clinical signs of shock had disappeared.

Mottled cyanosis of both legs was noted immediately after operation but was not so marked as in Case 1. Pitting edema of both legs and thighs was evident 4 hours after operation. The edema became most marked 36 hours after operation, after which it gradually subsided and remained absent as long as the patient was confined to bed. As soon as he was allowed out of bed, however, the edema returned, although it became progressively less each day. At the time of discharge only slight edema of the ankles and lower legs was present after the patient had been out of bed for some hours.

For the 4 days preceding caval ligation the temperature had fluctuated between 101 and 103°F. Within 5 hours after ligation the temperature fell to normal, where it remained for the next 36 hours. Beginning on the 2nd and continuing through the 8th postoperative day, the temperature fluctuated between 99 and 101°F, thereafter returning to normal where it remained during the rest of the hospital stay.

Use of the oxygen tent was continued through the first 48 hours after operation while the respirations were labored and rapid. Thereafter the respirations were normal in rate and excursion, and the oxygen was discontinued. The patient was then able to take food and fluids by mouth, so that intravenous medication was also discontinued.

On the 4th postoperative day, the patient was allowed to dangle his legs and the following day was allowed out of bed. In spite of rather marked weakness this activity seemed beneficial and was continued. On the 9th day, a considerable

crease in the amount of edema of the legs was noted. Examination of the abdomen showed a small amount of intraperitoneal fluid. Digitalization, which had been begun at the onset of the respiratory distress 5 days before operation, was continued. By the 12th postoperative day the edema and ascites had become worse and 1 cc of Salvirgan-Theophylline was given intravenously. This was followed by diuresis and diminution of both the ascites and the edema. Because this medication was followed by a chill and fever that lasted for several hours, it was not repeated. With continued activity the ascites gradually disappeared and at the time of discharge from the hospital was entirely gone. The ascites, associated with albuminuria, raised the question whether thrombosis of the inferior vena cava was extending from the site of ligation upward to the region of the renal vessels and possibly beyond. Judging from the subsequent course of events, it is improbable that this occurred.

During hospitalization venous-pressure studies were carried out using small veins on the dorsum of the foot or ankle, simultaneous readings being taken from the right arm. All veins were at the level of the heart when the pressures were recorded. The results of these studies are shown in Table 2.

TABLE 2 Venous-Pressure Readings

NO OF DAYS AFTER OPERATION	VENOUS PRESSURE		
	RIGHT FOOT mm. water	LEFT FOOT mm. water	RIGHT ARM mm. water
3	380	314	78
7	330	292	82
15	300	226	62

The progressive fall in the venous pressure of the feet indicates the rate at which the collateral circulation was established around the point of caval interruption.

Three months after operation the edema of the left leg was minimal and there was no edema of the right leg. All symptoms of obstruction of the bladder neck had disappeared after a prolonged course of stilbestrol,¹⁸ and there was no evidence of ascites. Enlarged veins were noted over the abdomen and chest, being particularly prominent over the lateral aspects.

SUMMARY AND CONCLUSIONS

Ligation of the inferior vena cava below the level of the renal veins, although an operation of some magnitude, is compatible with recovery in seriously ill patients.

Caval interruption is effective in preventing the embolic sequelae of thrombosis of the pelvic veins, whether this thrombosis is primary in the pelvic veins or secondary to a propagating thrombophlebitis originating in the veins of the legs.

Even following ligation of the common femoral veins, an adequate collateral circulation develops around the obstructed cava and peripheral edema eventually disappears.

The indications for ligation of the inferior vena cava are briefly discussed.

Two cases are presented in which caval interruption effectively prevented further pulmonary infarction. The operation was followed by complete recovery in each case.

The postoperative course in these cases is presented in some detail. The following points were most helpful in sustaining the patient through the critical postoperative period: swathing the feet, legs and thighs tightly in elastic bandages to help prevent shock due to the rapid withdrawal of edema fluid from the circulation, the early use of oxygen, and adequate intravenous infusions of plasma and whole blood.

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THE HAZARD OF TRANSFUSION MALARIA AFTER THE WAR

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ACCIDENTAL malaria subsequent to blood transfusion has not been a frequent occurrence in nonendemic areas. Since 1929 only 12 such cases have been reported to the Massachusetts Department of Public Health. In some other parts of the globe this route of transmission is more frequent. In Peiping, China, for example, Wang and Lee¹ reported 54 cases of malaria complicating 3700 transfusions over a period of ten years. Thoroughman,² working in Kiangsu, China, where malaria is encountered throughout the year, reported 45 cases of malaria after the administration of whole blood to 104 patients. In such endemic areas it is practically impossible to exclude mosquito

It is extremely likely that unless certain precautions are observed the situation after the war with reference to the paucity of malarial cases following transfusion will be considerably altered. In the first place, familiarity with the technic of administering whole blood as well as some of its derivatives has been acquired by large numbers of physicians serving with the armed forces. Furthermore, the available supply of whole blood in civilian hospital banks has increased tremendously during the war emergency.

At the conclusion of the war, large numbers of men will return to this country from regions in which malaria is endemic. A certain proportion of

TABLE 1. Post-Transfusion Malaria in Massachusetts (1929-1944)

CASE NO	AGE	SEX	TYPE OF MALARIA	INCUBATION PERIOD	DONOR	
					ENDEMIC COUNTRY KNOWN OF RESIDENCE	DURATION OF LATENCY
				days		yr
1	21	F	Quartan	89	Rumania	—
2	27	F	Quartan	46	Italy*	—
3	30	F	Quartan	49	—	—
4	4	F	Quartan	42	Italy	12
5	23	F	Quartan	—	—	—
6	49	M	Quartan	26	Greece	27
7	7	M	Quartan	21	Palestine†	—
8	3	M	Quartan	111	Albania	25
9	61	M	Quartan	31	Panama	20
10	41	F	Tertian	10	China‡	—
11	51	M	Tertian	21	Italy	—
12	4 months	F	Not stated	?	Greece	15

*History of malaria 10 years previously

†History of malaria 18 years previously

‡History of malaria 5 years previously

transmission in cases occurring after transfusion. Furthermore, consideration must be given in these localities to the possibility of a previously unrecognized latent infection as the cause of manifest malaria after a transfusion.

In nonindigenous areas where insect-borne malaria is exceedingly rare, difficulties of this sort are not encountered in the diagnosis of post-transfusion malaria. In Massachusetts, since 1930, the possibility of insect transmission within the Commonwealth was present in only 11 reported cases of malaria.³ Since 1938, not a single naturally acquired infection has originated in Massachusetts, but from 1939 to 1944 half the 12 post-transfusion cases were reported. This suggests that during the last six years the risk of acquiring malaria in Massachusetts by a blood transfusion has been greater than that by the natural route of infection. It is therefore apparent that observations in Massachusetts concerning accidental transmission as the result of transfusion are highly reliable.

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these persons will continue to harbor malarial parasites in the blood as the result of either clinical or subclinical infection. Although an increase of insect-borne malaria is not anticipated in this climate following the return of these men,⁴ it is conceivable that if such discharged veterans are used indiscriminately as whole-blood donors an increased incidence of post-transfusion malaria will be the result.

To re-emphasize the hazard of acquiring malaria as a result of either the intravenous or the intramuscular administration of whole blood, this paper will review the Massachusetts cases infected in this manner. In addition, the clinical and epidemiologic data concerning 2 of the more recent cases will be presented in detail.

SUMMARY OF CASES

The organisms identified in the blood smears of the 12 recipients were reported as follows: *Plasmodium malariae*, 9, *P. vivax*, 2, and type not stated, 1 (Table 1). The predominance of the quartan variety was striking. The clinical charts of all the cases except one demonstrated regularly recurring paroxysms every seventy-two hours. In Case 12,

that of a four-month-old child who developed malaria after several intramuscular injections of whole blood, the temperature rose every third day, with a low-grade fever intervening. It is well known that in infants and very young children the paroxysms may not be so clearly defined as they are in adults. Although the specific variety of plasmodium was not determined in this case, the long period of latency in the donor suggests that this, too, was quartan malaria.

The interval between the transfusion and the onset of symptoms in the recipient varied from ten days in Case 10 (tertian malaria) to one hundred and eleven days in Case 8 (quartan malaria). In the only other case of tertian malaria the incubation period was twenty-one days. Of the 8 quartan cases in which the incubation period could be determined, in 5 at least forty-two days elapsed before the first evidence of infection in the recipient. The patient in Case 5 received a series of transfusions for a period of several weeks before coming down with malaria, for this reason the incubation period could not be established.

The ages of the recipients varied from four months to sixty-one years. Seven patients were females, and 5 were males.

The ability of transfused blood to produce malaria is an indication of latency of infection in the donor. The total duration of latency is often difficult to establish. If the donor continues to reside in an endemic area subsequent to clinical malaria, the possibility of reinfection at a later date cannot be ruled out. Whether or not the donor presents a past history of malaria while living in an indigenous region, the duration of residence in a new country where insect transmission does not exist or is exceedingly rare may be regarded as the known period of latency. According to such a criterion, the known period of latency was established in 5 donors and varied from twelve to twenty-seven years (Table 1). Not one of these donors had a past history of manifest malaria.

Three additional donors presented a past history of malaria — one five years before infecting the recipient, the second ten years, and the third eighteen years. Because the duration and actual place of residence in the United States after being in an endemic region was not determined for these cases, the known period of latency could not be stated.

Of the 12 donors involved in this study, 10 had lived for a period of years in a country where malaria is known to be endemic (Table 1) — 3 in Italy, 2 in Greece and 1 each in Albania, China, Palestine, Panama and Roumania. In the other 2 cases, information concerning the donor's country of residence was not available.

Attempts to demonstrate malarial parasites in blood smears of the donor were made in 7 cases but were successful in only 2 (Cases 7 and 12). In most of these, both thick and thin smears were

examined. In 3 cases efforts to identify the plasmodium were unsuccessful in spite of splenic massage and the administration of adrenalin.

CASE REPORTS

CASE 1 M E, a 61-year-old native-born man, was admitted to the hospital on December 12, 1944, complaining of chills and fever of 3 weeks' duration. On October 16, a large tumor (cavernous hemangioma) had been removed from his back at another hospital. During the course of the operation and shortly thereafter the patient received several transfusions. He left the hospital on October 25. On October 30 he was readmitted because of sepsis in the operative wound. Healing occurred after incision, drainage and treatment with penicillin. He was discharged on November 14. On November 22 he began having daily chills, followed by sweats, usually late in the afternoon or evening. During the attacks he complained of severe headache.

The temperature on admission was 98.9° F, the pulse 72, and the respirations 18. Physical examination revealed a well-healed scar on the back where the tumor had been removed. There were no other unusual findings.

On December 13 the red-cell count was 4,240,000 and the hemoglobin, 81 per cent. The white-cell count was 5900, with 56 per cent neutrophils and 44 per cent lymphocytes. A blood culture on December 14 was negative, and a series of blood smears on December 13 and December 14 were positive for *P. malariae*. This was confirmed by the State Diagnostic Laboratory. X-ray examination of the chest showed evidence of chronic bronchitis in both lungs. Urinalysis was negative.

At least one paroxysm occurred each day, usually in the evening, from the day of admission until December 16. Antimalarial therapy with 1½ gr of atabrine three times daily was instituted on December 14. On December 16, 5 gr of quinine sulfate was also given the patient receiving this combination of drugs three times daily for the rest of the hospital stay. The temperature during the paroxysms varied from 100 to 101.4° F. Following treatment with quinine and atabrine the paroxysms disappeared. The temperature was 100° F on the morning of December 16, and except for a slight rise to 99.6° F in the evening of December 17 was normal thereafter. Antimalarial therapy was continued for an additional 4 weeks. Convalescence was uneventful, and the patient was discharged on December 20.

During the initial admission for the operation the patient received six transfusions, of which four were whole blood and two were plasma. It was determined that the donor for the transfusion given on October 20 had had an illness of 3 or 4 weeks' duration while living in Panama 20 years previously. The outstanding feature of this illness comprised recurrent paroxysms of chills and sweats. Physical examination of this donor revealed a palpable spleen. Thin and thick blood smears were examined after the injection of 1 cc. of adrenalin. Malarial parasites could not be found. Residence in an endemic country was denied by each of the other donors.

No cases of malaria had been reported from the recipient's community of residence for 15 years.

CASE 2 J K, a 3-year-old, native-born boy, visited his physician on October 17, 1944, with complaints of recurrent paroxysms of fever, chills and sweats every 72 hours for the last 6 weeks. About September 1, his mother noticed that he was not quite well. He was less active than usual and on one or two occasions was feverish. This was followed by the onset of regularly recurring paroxysms of chills and sweats every 3rd day.

The temperature, pulse and respirations were normal at the time of the initial examination. Physical examination revealed a pale, somewhat listless boy. The spleen was felt 3 fingerbreadths below the left costal margin. There were no other abnormal findings.

The patient's mother informed the attending physician that she expected the child to have a chill at 2 p.m. on the afternoon of October 19. One half-hour before this time the doctor visited the patient at his home. At the prophesied time a paroxysm occurred. Blood smears were taken immediately before the chill and shortly afterward. These were reported positive for *P. malariae* by the State Diagnostic Laboratory. Antimalarial therapy, consisting of quinine

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ACCIDENTAL malaria subsequent to blood transfusion has not been a frequent occurrence in nonendemic areas. Since 1929 only 12 such cases have been reported to the Massachusetts Department of Public Health. In some other parts of the globe this route of transmission is more frequent. In Peiping, China, for example, Wang and Lee¹ reported 54 cases of malaria complicating 3700 transfusions over a period of ten years. Thoroughman,² working in Kiangsu, China, where malaria is encountered throughout the year, reported 45 cases of malaria after the administration of whole blood to 104 patients. In such endemic areas it is practically impossible to exclude mosquito

It is extremely likely that unless certain precautions are observed the situation after the war with reference to the paucity of malarial cases following transfusion will be considerably altered. In the first place, familiarity with the technic of administering whole blood as well as some of its derivatives has been acquired by large numbers of physicians serving with the armed forces. Furthermore, the available supply of whole blood in civilian hospital banks has increased tremendously during the war emergency.

At the conclusion of the war, large numbers of men will return to this country from regions in which malaria is endemic. A certain proportion of

TABLE 1 Post-Transfusion Malaria in Massachusetts (1929-1944)

CASE No	AGE	SEX	TYPE OF MALARIA	INCUBATION PERIOD	DONOR	
					ENDEMIC COUNTRY OF RESIDENCE	KNOWN DURATION OF LATENCY
				days		yr
1	21	F	Quartan	89	Rumania	—
2	27	F	Quartan	46	Italy*	—
3	30	F	Quartan	49	—	—
4	4	F	Quartan	42	Italy	12
5	23	F	Quartan	—	—	—
6	49	M	Quartan	26	Greece	27
7	7	M	Quartan	21	Palestine†	—
8	3	M	Quartan	111	Albania	25
9	61	M	Quartan	31	Panama	20
10	41	F	Tertian	10	China‡	—
11	51	M	Tertian	21	Italy	—
12	4 months	F	Not stated	?	Greece	15

*History of malaria 10 years previously
†History of malaria 18 years previously
‡History of malaria 5 years previously

transmission in cases occurring after transfusion. Furthermore, consideration must be given in these localities to the possibility of a previously unrecognized latent infection as the cause of manifest malaria after a transfusion.

In nonindigenous areas where insect-borne malaria is exceedingly rare, difficulties of this sort are not encountered in the diagnosis of post-transfusion malaria. In Massachusetts, since 1930, the possibility of insect transmission within the Commonwealth was present in only 11 reported cases of malaria.³ Since 1938, not a single naturally acquired infection has originated in Massachusetts, but from 1939 to 1944 half the 12 post-transfusion cases were reported. This suggests that during the last six years the risk of acquiring malaria in Massachusetts by a blood transfusion has been greater than that by the natural route of infection. It is therefore apparent that observations in Massachusetts concerning accidental transmission as the result of transfusion are highly reliable.

these persons will continue to harbor malarial parasites in the blood as the result of either clinical or subclinical infection. Although an increase of insect-borne malaria is not anticipated in this climate following the return of these men,³ it is conceivable that if such discharged veterans are used indiscriminately as whole-blood donors an increased incidence of post-transfusion malaria will be the result.

To re-emphasize the hazard of acquiring malaria as a result of either the intravenous or the intramuscular administration of whole blood, this paper will review the Massachusetts cases infected in this manner. In addition, the clinical and epidemiologic data concerning 2 of the more recent cases will be presented in detail.

SUMMARY OF CASES

The organisms identified in the blood smears of the 12 recipients were reported as follows: *Plasmodium malariae*, 9, *P. vivax*, 2, and type not stated, 1 (Table 1). The predominance of the quartan variety was striking. The clinical charts of all the cases except one demonstrated regularly recurring paroxysms every seventy-two hours. In Case 12,

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that of a four-month-old child who developed malaria after several intramuscular injections of whole blood, the temperature rose every third day, with a low-grade fever intervening. It is well known that in infants and very young children the paroxysms may not be so clearly defined as they are in adults. Although the specific variety of plasmodium was not determined in this case, the long period of latency in the donor suggests that this, too, was quartan malaria.

The interval between the transfusion and the onset of symptoms in the recipient varied from ten days in Case 10 (tertian malaria) to one hundred and eleven days in Case 8 (quartan malaria). In the only other case of tertian malaria the incubation period was twenty-one days. Of the 8 quartan cases in which the incubation period could be determined, in 5 at least forty-two days elapsed before the first evidence of infection in the recipient. The patient in Case 5 received a series of transfusions for a period of several weeks before coming down with malaria, for this reason the incubation period could not be established.

The ages of the recipients varied from four months to sixty-one years. Seven patients were females, and 5 were males.

The ability of transfused blood to produce malaria is an indication of latency of infection in the donor. The total duration of latency is often difficult to establish. If the donor continues to reside in an endemic area subsequent to clinical malaria, the possibility of reinfection at a later date cannot be ruled out. Whether or not the donor presents a past history of malaria while living in an indigenous region, the duration of residence in a new country where insect transmission does not exist or is exceedingly rare may be regarded as the known period of latency. According to such a criterion, the known period of latency was established in 5 donors and varied from twelve to twenty-seven years (Table 1). Not one of these donors had a past history of manifest malaria.

Three additional donors presented a past history of malaria — one five years before infecting the recipient, the second ten years, and the third eighteen years. Because the duration and actual place of residence in the United States after being in an endemic region was not determined for these cases, the known period of latency could not be stated.

Of the 12 donors involved in this study, 10 had lived for a period of years in a country where malaria is known to be endemic (Table 1) — 3 in Italy, 2 in Greece and 1 each in Albania, China, Palestine, Panama and Roumania. In the other 2 cases, information concerning the donor's country of residence was not available.

Attempts to demonstrate malarial parasites in blood smears of the donor were made in 7 cases but were successful in only 2 (Cases 7 and 12). In most of these, both thick and thin smears were

examined. In 3 cases efforts to identify the plasmodium were unsuccessful in spite of splenic massage and the administration of adrenalin.

CASE REPORTS

CASE 1 M E, a 61-year-old native-born man, was admitted to the hospital on December 12, 1944, complaining of chills and fever of 3 weeks' duration. On October 16, a large tumor (cavernous hemangioma) had been removed from his back at another hospital. During the course of the operation and shortly thereafter the patient received several transfusions. He left the hospital on October 25. On October 30 he was readmitted because of sepsis in the operative wound. Healing occurred after incision, drainage and treatment with penicillin. He was discharged on November 14. On November 22 he began having daily chills, followed by sweats, usually late in the afternoon or evening. During the attacks he complained of severe headache.

The temperature on admission was 98.9° F, the pulse 72, and the respirations 18. Physical examination revealed a well-healed scar on the back where the tumor had been removed. There were no other unusual findings.

On December 13 the red-cell count was 4,240,000 and the hemoglobin, 81 per cent. The white-cell count was 5900, with 56 per cent neutrophils and 44 per cent lymphocytes. A blood culture on December 14 was negative, and a series of blood smears on December 13 and December 14 were positive for *P. malariae*. This was confirmed by the State Diagnostic Laboratory. X-ray examination of the chest showed evidence of chronic bronchitis in both lungs. Urinalysis was negative.

At least one paroxysm occurred each day, usually in the evening, from the day of admission until December 16. Antimalarial therapy with 1½ gr of atabrine three times daily was instituted on December 14. On December 16, 5 gr of quinine sulfate was also given the patient receiving this combination of drugs three times daily for the rest of the hospital stay. The temperature during the paroxysms varied from 100 to 101.4° F. Following treatment with quinine and atabrine the paroxysms disappeared. The temperature was 100° F on the morning of December 16, and except for a slight rise to 99.6° F in the evening of December 17 was normal thereafter. Antimalarial therapy was continued for an additional 4 weeks. Convalescence was uneventful, and the patient was discharged on December 20.

During the initial admission for the operation the patient received six transfusions, of which four were whole blood and two were plasma. It was determined that the donor for the transfusion given on October 20 had had an illness of 3 or 4 weeks' duration while living in Panama 20 years previously. The outstanding feature of this illness comprised recurrent paroxysms of chills and sweats. Physical examination of this donor revealed a palpable spleen. Thin and thick blood smears were examined after the injection of 1 cc of adrenalin. Malarial parasites could not be found. Residence in an endemic country was denied by each of the other donors.

No cases of malaria had been reported from the recipient's community of residence for 15 years.

CASE 2 J K, a 3-year-old, native-born boy, visited his physician on October 17, 1944, with complaints of recurrent paroxysms of fever, chills and sweats every 72 hours for the last 6 weeks. About September 1, his mother noticed that he was not quite well. He was less active than usual and on one or two occasions was feverish. This was followed by the onset of regularly recurring paroxysms of chills and sweats every 3rd day.

The temperature, pulse and respirations were normal at the time of the initial examination. Physical examination revealed a pale, somewhat listless boy. The spleen was felt 3 fingerbreadths below the left costal margin. There were no other abnormal findings.

The patient's mother informed the attending physician that she expected the child to have a chill at 2 p.m. on the afternoon of October 19. One half-hour before this time the doctor visited the patient at his home. At the prophesied time a paroxysm occurred. Blood smears were taken immediately before the chill and shortly afterward. These were reported positive for *P. malariae* by the State Diagnostic Laboratory. Antimalarial therapy, consisting of quinine

sulfate, was instituted immediately. The paroxysm that was expected on October 22 did not occur. Antimalarial treatment was continued for a period of 5 weeks, during which time there were no recurrences. The spleen gradually diminished in size and was no longer palpable at an examination 2 months after the onset of treatment.

Careful inquiry into the history of this patient revealed that he had received a transfusion of 300 cc of blood from his father on May 12 because of a severe infection of the throat. The father presented no history of malaria. He was born in Albania in 1899 and came to this country in December, 1919. During his 25 years' residence here he had been perfectly well. Thick and thin smears of the donor's blood were negative for *P. malariae*. Adrenalin was not administered.

Malaria had not been reported from the community where this case had occurred for nineteen years.

DISCUSSION

Although quartan malaria in most parts of the world occurs less frequently than either the tertian or estivoautumnal varieties,⁴ it is noteworthy that in this series of 12 cases of post-transfusion infection at least 9 and possibly 10 were caused by *P. malariae*. It is known that the period of latency in tertian infections may endure for about five years and that a single falciparum infection may remain latent for one month to a year.⁴ Evidence of the sort presented in this paper indicates that latency in quartan malaria is of much greater duration.

When the war is over, the majority of malaria carriers returning from endemic areas will harbor *P. vivax*. If such persons are used as whole-blood donors within five years of their return, an increase in post-transfusion malaria of the tertian variety may occur. If large numbers of troops remain indefinitely in endemic areas, the potential supply of tertian carriers who return to this country will remain at a high level for a long time after the war. A rise in tertian cases as a result of accidental transmission may become a serious problem for a period of several years.

This possible increase in incidence in the post-war period may be prevented by rejecting all prospective donors for whole-blood transfusion who have served in endemic malarious regions. Prophylactic administration of quinine or atabrine while in the endemic area or the absence of a history of malaria should not alter this rule. Obviously, when blood is being drawn for plasma this precaution is not essential.

Ackermann and Filatov⁵ and Antschelewitsch⁶ have shown that when blood is stored for a long time plasmodia gradually degenerate and finally disappear. The former investigators, working with psychotic patients, were unable to transmit malaria with whole blood stored in the refrigerator for five days or longer. Antschelewitsch was able to infect persons with whole blood stored for eight days. One of our cases (Case 5) occurred after a series of stored-blood transfusions.

The long interval between the transfusion and the onset of symptoms observed in several of these

cases deserves further comment. Although the incubation period in malaria varies in naturally acquired infections from six to forty days, longer periods have occasionally been reported. In Holland it has been observed that outbreaks each spring are due to infections contracted during the previous autumn.⁷ Schuffner and Schwellengrebel (quoted by Hackett⁴) allowed themselves to be bitten by infected mosquitoes in the fall and had their onset eight or nine months later. It may be postulated that the prolonged incubation period noted in several of our patients was due to the relatively small number of parasites in the circulating blood after a long period of latency.

Because several weeks may elapse between the transfusion and the onset of malaria in the recipient, the causal relations of these events may not be recognized. Stein⁸ reported a case in which such an association was not realized after the transfusion of a girl with blood from her father. The patient recovered after treatment with quinine. Following a second transfusion from the same donor, she again became ill with malaria. At that time it was discovered that the father had had malaria eight years previously, and parasites were demonstrated in his blood after the second transfusion.

Post-transfusion malaria when recognized and promptly treated is not usually fatal. It is an infection that may be prevented by properly selecting donors for blood transfusion. Simply by exercising care in this respect, an increase in the incidence of post-transfusion malaria after the war can be prevented.

SUMMARY

Since 1929, of 12 cases of post-transfusion malaria reported in Massachusetts, 9 were quartan, 2 tertian, and 1 undetermined.

The predominance of quartan infections is evidence that in a nonendemic area the problem of post-transfusion malaria is intimately linked with the ability of *Plasmodium malariae* to remain latent for long periods of time.

Because of the absence of insect-borne transmission in a nonendemic area, latency may be determined with a greater degree of accuracy in such an area than in an endemic one in which reinfection is difficult to exclude.

The widespread use of whole-blood transfusions in medical practice and the return to this country of large numbers of carriers from endemic areas may act together to increase the hazard of accidental transmission of malaria in the post-war period.

An increased incidence of tertian malaria as a result of accidental transmission may be prevented after the war by eliminating prospective donors for whole-blood transfusions who have lived in endemic areas.

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CLINICAL NOTE

GASTROSCOPIC STUDIES IN NAVAL PERSONNEL WITH CHRONIC SEASICKNESS*

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In a group of 150 cases of chronic seasickness studied clinically at the United States Naval Hospital in Chelsea, Massachusetts,^{1,2} routine gastrointestinal x-ray studies showed that 50 per cent had a characteristic roentgenologic appearance.³ These cases showed a constant triad of findings, namely, hypersecretion, loss of gastric motility and spasm of the pylorus. In a few cases there was in addition evidence of a moderate degree of hypertrophic gastritis, seen when a thick barium solution was used to bring out the gastric rugae.

It was considered highly desirable to confirm these findings by direct gastroscopic examination. Since facilities for this examination were not available at the naval hospital, it was performed at the Gastroscopic Clinic of the Massachusetts General Hospital. The patients did not receive breakfast or lunch on the day of the examination and were usually given 0.1 gm. of Nembutal on leaving the naval hospital, so that a mild degree of relaxation was possible when they reached the civilian clinic. They were for the most part examined within five days of being sent ashore from the small vessels on which they had been seasick. They had had from four to six weeks of protracted seasickness, with extreme vomiting, weight loss and a decrease in efficiency.

The results of gastroscopic examination in 22 men showed moderate hypertrophic gastritis (1 case), moderate superficial gastritis (2 cases), slight superficial gastritis (3 cases), gastric spasm without gas-

tritis (2 cases) and a normal stomach (14 cases). As pointed out by Benedict and Mallory,⁴ superficial gastritis as described by the gastroscopist corresponds to the acute exudative gastritis of the pathologist. Hypertrophic gastritis as described gastroscopically corresponds to an exaggerated form of the physiologic plasma-cell and lymphocytic infiltration of the normal stomach (chronic gastritis).

Most of the patients were under twenty-five years old, an age group in which one would expect to find a comparatively normal gastric mucosa. Although a series of 22 cases is too small a one from which to draw any final conclusions, the finding of a normal stomach in 14 of them indicates that seasickness does not usually cause changes in the gastric mucosa.† The only patient showing any degree of chronic (hypertrophic) gastritis was a man of forty-one who had suffered mild seasickness before joining the Navy and had then suffered two months of severe perpetual seasickness. Two other patients had spasm without gastritis, and 3 of the remaining 5 showed only slight superficial gastritis, which in 2 cases was confined to a small area. In 1 of the latter cases, re-examination six weeks later revealed a normal stomach. Of the 2 patients who showed moderate superficial gastritis, 1 was a habitual user of alcohol. Hence, the thickened rugae observed by x-ray examination in many of these cases were not confirmed by gastroscopy and cannot be considered as positive evidence of gastritis.

CONCLUSION

Although 50 per cent of cases of chronic seasickness present x-ray evidence of hypersecretion, loss of gastric motility and spasm of the pylorus, as well as thickened gastric rugae in some, the gastroscopic picture is usually essentially normal.

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†The cases reported herein are not to be confused with those of so-called destroyer stomach, which usually exhibit severer and more prolonged pain and distress. Such patients also frequently have x-ray evidence of thickened gastric rugae, but in only half of these cases does gastroscopy reveal any degree of gastritis.

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MEDICAL PROGRESS

PRACTICAL ASPECTS OF OXALATE METABOLISM (Concluded)*

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OXALATE LITHIASIS

Urinary lithiasis is a broad subject. There are a number of excellent general papers that are of considerable value for the purpose of orientation in this complex field.⁸²⁻⁸⁹ There has been an increasing interest in recent years in the pathogenesis of urinary calculi. Many factors, such as hyperparathyroidism, persistent hypercalciuria, urinary-tract stasis, a persistently alkaline urine, infection

stone is well shown in Table 2, which is based on the chemical analysis of stones as reported by several authorities.⁹¹⁻⁹⁶ Barney and Jones⁸⁸ state that from 1936 to 1940 analysis of stones removed at operation or passed spontaneously at the Massachusetts General Hospital showed phosphates in 59 per cent and oxalates in 33 per cent. Burkland⁹⁰ reports that among 112 cases of urinary-tract calculi analyzed at the Brady Urological Institute the

TABLE 2 Frequency of Various Types of Urinary Calculi *

TYPE OF STONE	RANDALL ⁹⁵		KRETSCHMER ⁹⁴	LA TOWERS ⁹⁶	McINTOSH ⁹¹
	KIDNEYS	URETER	URETER	ENTIRE URINARY TRACT	ENTIRE URINARY TRACT
Calcium magnesium phosphate	39	49			
Calcium phosphate carbonate					9
Calcium phosphate			47	13	
Calcium oxalate	11	39	39	33	50
Calcium carbonate	4	4	6	14	
Triple phosphates	7		4		
Magnesian†					29
Cystine	4	1	3	2	1
Uric acid and urates	6	7	1	10	11
Miscellaneous pure stones			2	6	
Mixed stones	80	59		72	
Totals	151	159	102	150	100

*The classification of stones varied with each author. Pure stones were generally considered to be those with a predominance of one or in some cases two elements. McIntosh's classification is chiefly based on the presence or absence of the metallic elements.

†Magnesian stones contain not only calcium carbonate and calcium phosphate but also magnesium and ammonium.

of the urinary tract with urea-splitting organisms and prolonged recumbency, have been established as causes of phosphate calculi. Furthermore, the prevention of their recurrence and even their dissolution by chemical means have had some measure of success. By contrast, the pathogenesis and therapy of oxalate calculi remain enigmatic. Burkland⁹⁰ has given the best modern appraisal of the problem. This paper and those by McIntosh⁹¹ and Hammarsten⁹²⁻⁹³ should stimulate a renewed interest in oxalate calculi.

One of the most important aspects of oxalate metabolism is its role in the causation of calculi in the urinary tract. Oxalate stones occur both in a relatively pure form as calcium oxalate and as mixed stones. They are exceedingly frequent and are therefore of considerable clinical interest. Their frequency as contrasted with that of other types of

were 62 in which the stones were composed of pure calcium oxalate or of calcium oxalate and phosphate. Thompson et al.⁹⁷ report that the quantitative chemical analysis of urinary calculi in 47 cases revealed 78 per cent to be of the calcium oxalate-phosphate type, with the heavy calculi containing more phosphate and those of light weight relatively richer in oxalate. It thus appears that in the United States more than 30 per cent of all stones of the urinary tract are of oxalate origin. The incidence of mixed oxalate stones is high, since calcium oxalate occurs in acid urine in association with uric acid and urates and in alkaline urine with amorphous phosphates. Predominant calcium oxalate stones develop only in acid urine.^{90, 91} Because of their frequent small size oxalate stones often enter the ureter and make up a large percentage of ureteral stones. Because of their rough surface they frequently cause colic and hematuria. In the so-called "stone belt" of Central Europe (see below) the percentage of oxalate stones is said to reach 65 per cent of all urinary tract calculi.^{98, 99}

Oxalate calculi occur in several forms¹⁰⁰⁻¹⁰²—as small, smooth, round or faceted stones, not larger

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than a pea and usually found in the renal pelvis or ureter, as "mulberry calculi," so named because of mammillary processes on their surfaces, of larger size and more frequent in the bladder, as those of so-called "jackstone shape," a rare type with projecting spurs, seen in the bladder, and as crystalline calculi, small stones with their surfaces completely covered with sharp, glistening crystals, which are exceedingly irritating. Many of the small oxalate stones passed naturally or found at operation in persons with uninfected urine are of the last type. In contrast to those composed of calcium phosphate and cystine, staghorn calcium oxalate calculi are rare.

Calcium oxalate calculi are extremely dense and readily demonstrable on a K U B roentgenogram. The roentgen appearance of spicules radiating from a central focus is seen at times and is pathognomonic of this type of calculus (see illustration^{93 101}). According to the Schinz experiment, as tabulated by Morrison,¹⁰² the relative densities of urinary calculi on roentgen-ray examination are water and body tissue, 1, xanthine, 1.2, urates, 1.38, cystine, 3.7, ammonium magnesium phosphate, 4.1, calcium oxalate, 10.8, calcium carbonate, 15.0, and calcium phosphate, 22.0. Others rate calcium oxalate as the densest of all.^{90 100}

Heredity is not generally considered a factor in the pathogenesis of oxalate calculi. Nevertheless, there are isolated papers in which this possibility is considered. Gram¹⁰³ has reported the study of five generations of a family in which calcium oxalate urinary concretions occurred with great frequency. This predisposition to form calculi was apparently inherited dominantly but showed itself clinically almost exclusively in males.

Oxalate calculi may occur in acid, neutral or alkaline urine and remain insoluble in either acid or alkaline urine. It is also generally agreed that neither stasis nor infection of the urinary tract predisposes to the formation of calcium oxalate stones. This is in sharp contrast to calcium phosphate calculi.

There are a number of areas in the world where oxalate stones are particularly prevalent. In some of these the calculi appear to be related to a vegetable diet of high oxalic acid content. This is by no means constant, for in other equally prominent stone areas the diet is noticeably low in oxalates.^{89 98-100 104} Here the source of the urinary oxalates appears to be of intestinal or endogenous origin. A most remarkable phenomenon has been noted in the area of Central Europe blockaded during World War I.^{98 99} Starting about 1919, reaching a sharp peak in 1924 and remaining sustained until at least 1937, there was a striking increase in the incidence of oxalate stones, at times reaching ten times the usual incidence. Oxalate stones were said to constitute 65 to 90 per cent of all stones studied by urologists in this area. The stones were

small, renal in origin, often

and frequent in middle-aged

only infrequently. A careful ana-

etiologic factors led Grossmann^{98 99} to co-

the basic cause remained obscure. Wins-

White¹⁰⁵ suggested that a dietetic fault seemed

highly probable. Hammarsten's^{92 93} experimental

production of oxalate stones in rats on a diet low in

magnesium is a new concept that may possibly shed

some light on the reason for this stone wave. The

magnesium content of foods varies with the content

of this element in the soil. Prevention of its depletion

from the soil in turn depends on the agricultural

methods and type of fertilizer used.¹⁰⁶

Whether or not this can predispose toward human

oxalate lithiasis remains to be proved.

Many attempts have been made to associate

oxalate stones with oxaluria. Although this may in

general be true, it appears that oxaluria may per-

sist for years without oxalate stones' developing,

and conversely that oxalate stones are not always

associated with hyperoxaluria or demonstrable

oxalate crystals in the urine. The many factors in-

creasing the oxalate content of urine are discussed

below. It is not clear what role these have in the

production of oxalate stones. It has been stated

that persons with oxalate stones after eating foods

rich in oxalic acid occasionally show either an un-

usually high blood and urine oxalate content or one

less than the normal supply.⁹⁰ Such inconsistent

results make evaluation of this factor difficult.

Calcium oxalate in the normal urine is usually

supersaturated — from two and a half to three

and a half times at a pH of 5.5, according to Las-

sen,¹⁰⁷ to as much as six- to eightfold according

to others.^{100 106} Hydrotropic and colloidal sub-

stances present in the urine are undoubtedly respon-

sible for at least part of this increased solubility of

calcium oxalate as compared with its solubility in

distilled water. The influence of urea in increasing

the solubility of calcium oxalate in water is illus-

trative of this mechanism.^{108 109} It is therefore pos-

sible that the formation of oxalate stones depends

more on decreased solubility due to some disturbance

in such a protective colloidal mechanism than on

an absolute increase of urinary excretion of oxalates.

Unfortunately, but little is known concerning the

factors controlling the protective colloidal mecha-

nism. Furthermore, the primary role of this mecha-

nism has recently been questioned.⁹¹

The crystals formed in a colloid menstruum *in vitro*

differ from those of the same substance formed in a

watery solution.¹¹⁰ Ord and Shattock¹¹¹ showed

many years ago that the so-called "coalescent

forms" of oxalate crystals constituted the structural

units of oxalate calculi as seen microscopically.

Lassen¹⁰⁷ administered to patients a saline solu-

tion containing calcium, magnesium and phosphate

(Hammarsten's mixture) and a solution of sodium

chloride and magnesium chloride, with promotion of

diuresis and diminution in concentration of oxalate and an increase in magnesium and calcium in the urine. Consequently, the urine became less saturated with calcium oxalate. The therapeutic implication of this observation remains to be determined.

Small calcium oxalate stones with a single faceted area suggesting attachment and development from a primary lesion on a renal papilla have been noted on occasion.^{105, 112, 113} Although this may explain their origin, the continued growth of calculi apparently depends on other factors.

Much interest has been aroused in recent years in the relation of citric acid metabolism to renal calculi and the possible therapeutic value of the use of citrate or agents that control its urinary excretion in the management of calculi,¹¹⁴⁻¹¹⁷ as well as the use of aluminum hydroxide gels to divert phosphate excretion from the urinary to the intestinal tract.¹¹⁷ Citrate solutions containing magnesium used locally in the urinary tract have successfully dissolved stones.¹¹⁸ These new concepts, however, appear to be related to stones composed of phosphates or carbonates rather than of oxalates.

Oxalate calculi have been produced experimentally in animals. Renal calculi produced by vitamin A deficiency¹¹⁹ are composed of phosphates. The production of an intense artificial hyperoxaluria by administration of oxalic acid esters and salts subcutaneously in a carefully controlled experiment utilizing over 900 rats, Hammarsten^{92, 93} not only produced oxalate calculi but apparently elucidated some pathogenic factors involved. These striking results are worthy of careful attention and, since original papers are not readily accessible, will be discussed in some detail. A magnesium-poor diet induced oxalate stones, with or without an increase in intake of vitamins A and D, but the stones were more numerous with avitaminosis. Oxalates in the diet favored stone formation but was not essential, since calcium oxalate stones formed on an oxalate-free diet. Paradoxically, a diminution in calcium in the food increased elimination of calcium in the urine and was marked when the animal was deficient in calcium.

A low-magnesium, high-oxalate, low-phosphorus diet gave the highest incidence of stones. The stones of the urine of animals with experimental calcium oxalate calculi showed it to be acid with decreased magnesium content. The pH of the urine of these animals was 5.5 to 6.0, if the diet was high in oxalate. The pH of the urine of animals with stones was 6.5 to 7.0.

magnesium intake, which decreased the excretion of calcium oxalate, some ill-defined disturbance in metabolism due to the magnesium deficiency, a negative calcium balance and increased calcium excretion, and the excretion of more oxalic acid was obtained in the diet.

Increase of magnesium in the diet without an increase in vitamins caused a diminution in urinary calcium excretion. A vitamin-deficient diet together with a low calcium intake led to mobilization of calcium from the skeleton, with a negative calcium balance and high urinary calcium excretion. Increasing the amount of calcium in the diet apparently decreased the excretion of oxalic acid, increased the solubility of urinary calcium oxalate, and at the same time diminished urinary elimination of calcium.

Hammarsten also succeeded in decalcifying formed calculi. Animals were kept on the diet producing regime until roentgen-ray study revealed the presence of calculi. The diet was then changed to one rich in calcium, magnesium and all the vitamins. After several months, post-mortem examination of the sacrificed animals showed complete almost complete decalcification of the stones, with the organic matrix still present.

It is well to note that Hammarsten's work is confirmation, and further that it is not only applicable to man. The principles evolved in her experiments are applicable to man. The metabolism of oxalic acid and calcium and the role of the metallic elements in the metabolism of calcium oxalate stones. A great advance in our knowledge of the conditions underlying stone formation. Hammarsten's work is confirmed.

Burkland,⁹⁰ on the basis of available clinical evidence, suggests that the formation of oxalate stones in the urinary tract can be decreased by a well balanced diet, by increasing use of foods of high oxalic acid content, increased intake of vitamins A and B, by a diet of carbohydrates in the diet to cut down on fermentation and the production and absorption of oxalic acid, by eliminating constipation, chronic indigestion and so forth, by avoiding worry, by drinking eight to ten glassfuls of water daily, by eating relatively rich in proteins, by some form of exercise and by eliminating foci of infection. The paper contains a specimen dietary instruction sheet, the suitable for patients, that embodies the aforementioned ideas and a simplified table of oxalic acid content of foods.

Hammarsten,^{92, 93, 120} on the basis of her experiments, has suggested a prophylactic diet.

whole-grain products, a variety of fruits and vegetables (consumed raw or with water used for cooking), milk, butter, meat and meat broth. If necessary, medicinal calcium and magnesium can be used to supplement the diet. Magnesium is present in any natural foods, so that a well-balanced diet could furnish an adequate amount. There may be some loss in water used for cooking. The true value of these prophylactic regimes for preventing the formation of oxalate calculi in human beings remains to be adequately established, but for the present they can be considered to rest on a rational basis. It is well to recall, however, that the results obtained from animal experiments are not always directly applicable to man.

THE METABOLISM OF OXALATES

Blood and Urine Levels

There is considerable variation in the reported values for the normal oxalate content of the blood, as may be seen from Table 3, apparently depending to a great extent on the method used.¹²¹⁻¹³⁰ No attempt will be made to review or compare all the methods. Barrett¹³⁰ has recently evaluated results

TABLE 3 Normal Oxalate Content of the Blood

SOURCE	SPECIES	OXALATE CONTENT mg /100 cc
Merz and Mauger ¹²¹	Man	3.0
	Rabbit	6.0-9.0
Loeper ¹²²	Man	1.0 or less
Jürgens and Spehr ¹²²	Man	5.22-9.72
	Dog	5.40-19.26
Suzuki ¹²⁴	Man	4.0-6.0
Kamiya et al ¹²⁵	?	2.0-4.0
Steinberg and Brown ¹²⁸	Man	5.5-7.5
	Rabbit	4.5-6.0
Leulier and Dorché ¹²⁷	Horse	0.227-0.270
	Ox	0.218-0.276
	Sheep	0.268-0.485
Steinberg et al ¹²⁸	Man	5.0-7.5
Barber and Gallimore ¹²⁹	Man	0.4-0.6
	Rabbit	0.4-0.8
Barrett ¹³⁰	Man	0.23-0.77 (Average 0.48)

obtained by means of the three most widely used procedures, namely, the cerous chloride precipitation method of Izumi, Suzuki¹²⁴ and other Japanese investigators, the lime water precipitation method of Merz and Mauger¹²¹ and the ethyl oxalate procedure of Dodds and Gallimore.¹³¹ He was unable to confirm the high values obtained by the methods of the Japanese workers or of Merz and Mauger; he concluded that the low values obtained by Dodds and Gallimore were of the correct order of magnitude. Furthermore, he cast some doubt that the oxalate obtained by any procedure is entirely pre-existent oxalate, since the mere addition of ascorbic acid to blood prior to the determination increased the oxalate content by 0.025 mg for each 1 mg of ascorbic acid added. Some reported values for the oxalate content of urine are given in Table 4.¹³²⁻¹³⁶ These also are subject to question because of the

lack of reliability of the methods used, although there is a greater uniformity here than in the values reported for blood oxalate.

It is important to bear in mind in any evaluation of the published reports that the results are often open to question and not frequently are invalid.

Oxalate Values in Various Diseases

In addition to the hyperoxalemia and hyperoxaluria reported in the syndrome of oxaluria, there are numerous references to elevations in a variety of

TABLE 4 Normal Oxalate Content of the Urine

SOURCE	SPECIES	OXALATE CONTENT mg /24 hr
Loeper ¹²²	Man	20.0 mg (per liter)
Borgström ¹³²	Guinea pig	0.57-0.87
Herkel and Koch ¹³²	Rabbit	5.0-15.0
	Man	21.5 (average)
Müller ¹³³	Man(?)	20.0-40.0
Widmark ¹³⁴	Man	14.0-56.0
Okawa ¹³⁵	Rabbit	5.6-15.9
Adolph and Liang ¹³⁶	Rat	1.0
Barrett ¹³⁰	Man	20.0-47.0 (Average, 33 mg)

unrelated diseases. These reports are found almost entirely in the foreign literature, much of which is not available. Consequently, no attempt has been made to review this subject completely. References are made merely to certain illustrative papers to indicate the apparent wide scope of the subject.

Jürgens and Spehr¹²² found blood oxalate values elevated in diseases of the liver, with a tendency to parallel the serum bilirubin level. Pennetti¹³⁷ reported similar clinical findings and experimentally produced hyperoxalemia in rabbits and dogs by ligation of the common bile ducts. Herkel and Koch¹³² found high urinary values in a patient with cirrhosis of the liver without jaundice who was being maintained on a high-carbohydrate diet. In addition, they demonstrated that the ingestion of 600 to 800 gm of spinach (equivalent to 3 or 4 gm of oxalic acid) by 2 patients, one with cirrhosis of the liver with ascites and the other with cirrhosis with jaundice, caused a marked elevation in urinary oxalate content. This they attributed to an elevation in blood oxalate, although they made no determinations on the blood.

Scaglioni¹³⁸ found the blood oxalate level of patients with compensated cardiac disease to be normal. With development of edema and oliguria the blood level rose and the urinary excretion became relatively greater, although the total daily output was unaffected. With improvement of the cardiac status under routine therapy the blood oxalate values returned to normal. Loeper et al¹³⁹ noted similar findings in patients with varying degrees of cardiac failure. Simultaneously determined values for urinary oxalate convinced them that the oxalemia could not be explained on the basis of renal insufficiency.

Scaglioni¹⁴⁰ also investigated the level of blood and urine oxalates in various types of renal disease, with and without insufficiency. He found no variations from normal when renal function was normal, as tested by the blood nonprotein nitrogen and by concentration and dilution tests. With renal insufficiency the blood oxalate became elevated, but the urinary values varied from low to normal to high. If improvement occurred, however, the urinary oxalate increased as the blood oxalates returned to normal. Although the oxalate level of the blood tended to be high, it did not exactly parallel the intensity of the clinical manifestations. Khouri^{141, 142} and Jürgens and Spehr¹²² have reported hyperoxalemia, and Herkel and Koch¹³² have noted hyperoxaluria, in uremia.

A number of investigators^{122, 123, 143-145} report that diabetes mellitus is associated with hyperoxalemia oxaluria or both. Herkel and Koch¹³² however, were unable to find any relation between the urinary values for glucose and those for oxalic acid. The blood oxalate values parallel the blood sugar values and respond to insulin in a similar manner.

In addition, deviations from normal values have been noted in certain severe diseases of the central nervous system,¹⁴⁶ chronic nongouty arthritis,¹⁴⁷ gouty arthritis,¹⁴⁷ severe anemias¹⁴² and leukemia.¹⁴²

Source of Blood and Urine Oxalates

The oxalate of the blood and urine is derived from several sources not all of which have been adequately proved. The largest and best understood source is oxalate pre-existent in food. The oxalate content of certain foodstuffs has been listed in Table 1. This is present as insoluble calcium oxalate, as soluble sodium or potassium oxalate and in very slight amounts as oxalic acid. The calcium oxalate is relatively insoluble, is absorbed from the intestinal tract with great difficulty and is largely excreted in the feces. The degree to which it is absorbed is thought to be related to the gastric acidity and may be increased in the presence of hyperchlorhydria. Herkel and Koch¹³² studied the oxalate excretion in the urine after the administration of spinach. In normal persons increase occurred during the six hours following ingestion, but this response could be diminished by atropine and greatly enhanced by histamine. Patients with achlorhydria failed to show oxaluria after ingestion of spinach and were uninfluenced by histamine, but developed oxaluria if hydrochloric acid was administered with the spinach. From this they concluded that gastric acidity is an important factor in determining the degree of absorption of oxalates from the gastrointestinal tract. The soluble oxalates present in foods may be absorbed as such or be changed to insoluble calcium oxalate by combination with calcium in the diet. Thus, it has been demonstrated that the addition of milk, calcium chloride or calcium carbonate to the diet prevents the oxaluria

that follows the ingestion of an oxalate-rich food. It is important to emphasize that the oxalic acid values listed in Table 1 are figures for total oxalates expressed as oxalic acid. They do not differentiate the relative proportions of readily absorbable or difficultly absorbable forms, and are therefore not necessarily indicative of ability to elevate the blood or urine oxalate levels.

In addition to preformed oxalate it has been suggested that certain foodstuffs are potential sources, since oxalates may be intermediary products in their metabolism (the so-called "oxaligenic foods of Loeper"). Of these the most important are carbohydrates, especially glycogen and starches (Loeper,⁸ Loeper et al.¹⁴³ and Oikawa¹⁴⁸). Pure protein—for example, gelatin and plasma—and fats are not considered as precursors of oxalate, but meat and foods rich in connective tissue rank next to carbohydrate. Herkel and Koch¹³² studied 11 patients on an oxalate-poor diet with a constant protein and varying carbohydrate and fat content. The results were not constant, but patients tended to have greater urinary oxalate excretion on high-carbohydrate diets than on low-carbohydrate ones. Jürgens and Spehr¹²² studied the blood sugar and oxalic acid levels of normal patients after the oral administration of glucose. They found that the blood oxalate level tended to parallel the glucose level. The peak was reached somewhat earlier on the oxalate curve, and the decline was somewhat slower. They suggested that the oxalemia reported to be present in many patients might be explained on a basis of low sugar tolerance.

Second to the oxalate of food (actual or potential), the metabolic processes of certain intestinal bacteria and parasites have been emphasized as sources of oxalate. Loeper et al.¹⁴³ refer to experiments by various observers that demonstrate the formation of oxalic acid during *in vitro* studies on species of *Aspergillus* and *Mucor* and on the colon bacillus. Finck¹⁴⁹ credits Guidiceandrea with establishing in 1933 for the first time a relation between intestinal parasitosis and oxaluria. He suggests that "toxins" from the parasites interfere with the metabolism of the liver and thereby cause hyperoxalemia. Khouri¹⁴¹ finds blood oxalates to be elevated frequently in patients with filariasis and bilharziasis, and postulates that a "toxin" diminishes the oxalolytic action of the liver. A relation between oxaluria and amebic dysentery has been emphasized.⁸³ Loeper⁸³ calls attention to the association of oxaluria with *Taenia* infestation and suggests that the source of the oxalate is the metabolism of the parasite within the intestine. He and Tonnet¹⁵¹ report on *in vitro* experiments that demonstrate that, during the metabolism of *Taenia*, glucose and oxalic acid are formed at the expense of glycogen. Finck¹⁴⁹ reviews the literature and reports 58 cases of oxaluria in which parasitic infestation was present as follows: 7 cases with *Lambia*, 2 with *Taenia* and 49 with

caris He reports that examination of the stools of these patients showed, in addition to the evidence of parasitic infestation, large numbers of calcium oxalate crystals and an increase in undigested starch granules He postulates that the parasites interfere with the normal functioning of the pancreas and thereby indirectly affect oxalic acid metabolism He states that the successful elimination of the parasites was accompanied by disappearance of oxaluria Buche¹⁵² comments on the frequent association of colon-bacillus bacteriuria and oxaluria McCinnin and Lombardi^{153 154} isolated a strain of colon bacillus that produced oxalic acid in vitro and caused oxaluria when administered in capsules to healthy subjects

A third source of blood and urinary oxalate is the intermediary metabolism of tissues This is by far the most controversial and confusing of all the aspects of the subject In view of the questionable reliability of the methods used and the doubtful accuracy of many of the reported experiments, it is impossible to evaluate the status of the problem on the basis for the concept of endogenous production of oxalate lies in the demonstration that animals and human beings maintained on supposedly oxalate-free diets or undergoing starvation experiments continue to excrete oxalic acid in the urine This finding has been verified by a number of observers—Herkel and Koch¹⁵² in rabbits, Borgström¹⁵⁵ in guinea pigs, Jürgens and Spehr¹⁵⁶ in dogs, Adolph and Liang¹⁵⁶ in rats and Herkel and Koch¹⁵² and Jürgens and Spehr¹⁵⁶ in man It has been suggested that oxalic acid is related in some mysterious manner to the metabolism of carbohydrate This originally arose from the fact that in vitro oxalic acid is produced by the action of nitric acid on glucose—hence the name "sugar acid" Loeper¹⁵⁵ considers tissue carbohydrate, especially glycogen, to be a potent source of oxalic acid He and his co-workers¹⁵⁶ report that experiments on slices from rabbit's liver and heart show that, as the tissue glycogen decreases, the glucose and oxalic acid increase In addition, Loeper¹⁵⁵ claims that the coexistence of hyperglycemia and hyperoxalemia in diabetic patients and the simultaneous response of each to insulin support the concept of a specific interrelation The previously mentioned experiments of Herkel and Koch and of Jürgens and Spehr tend to substantiate this idea Oikawa¹⁵⁷ reports an extensive literature showing that hyperglycemia induced by the injection of glucose or adrenalin is accompanied by hyperoxalemia and often by oxaluria His own experiments, although purporting to substantiate those of other observers, fail to show a significant effect of either glucose or adrenalin

In addition to the investigations on the interrelation of carbohydrates and oxalic acid metabolism, a variety of other substances have been studied Most of the work has been directed toward the discovery of oxalate precursors by means of the

determination of blood and urine oxalate after the administration of test substances Glucose,¹⁵⁴ aspartic acid,¹⁵⁴ asparagine,¹⁵⁴ ethylene glycol,¹⁵⁵ ethylene monoacetate,¹⁵⁸ glycine,¹⁵⁹ creatinine,¹⁵⁹ purines,¹⁵⁹ glyoxal¹²² and glycolic acid¹²² have been reported as leading to an increase in oxalic acid A decrease in oxalate is said to follow the administration of pyruvic acid¹⁵⁴ Glycine,¹⁵⁴ alanine,¹⁵⁴ glutamic acid,¹⁵⁴ butyric acid,¹⁵⁴ fructose¹²² and oxamide¹²² have been ineffective

Some evidence has accumulated that implicates purine and pyrimidine metabolism in the production of oxalic acid Rodillon⁷⁷ suggested a schema in which oxalic acid appeared as an end product of a series of reactions beginning with uric acid and progressing through alloxan, oxaluric acid and finally urea and oxalic acid It is perhaps of interest to note that alloxan, now widely used in the experimental production of diabetes, is a ureide of mesoxalic acid

In this country some support for the interrelation of pyrimidine and oxalic acid metabolism has been obtained from the work of Cerecedo and his associates¹⁵⁹⁻¹⁶² They fed to dogs various substances considered as possible intermediaries in pyrimidine metabolism and then measured the urea and the oxalic acid content of the urine Although aware of the inadequacy of the methods for the determination of oxalic acid, they concluded that their results had relative, if not absolute, significance Uracil, oxaluric acid, formyloxaluric acid, isobarbituric acid and isodialuric acid resulted in an elevation of urinary urea, and oxaluric acid also caused a rise in urinary oxalic acid In addition, parabanic acid caused an elevation of urinary oxalate but along with alloxan and alloxantin did not appear to be involved in the metabolism of uric acid As a result of these investigations, the authors suggested a schema beginning with uracil and progressing through isobarbituric acid, isodialuric acid and oxaluric acid to the end products, urea and oxalic acid This is an interesting series of experiments that apparently have been neither confirmed nor disproved It is interesting to speculate whether such a substance as thiouracil could give rise to oxalic acid

It is probably worth mentioning at this point that in the citric acid cycle postulated for the oxidative breakdown of pyruvate, a schema in which vitamin B is intimately involved, a number of dicarboxylic acids have been implicated¹⁶³ Thus, citric, α -ketoglutaric, succinic, fumaric, malic and oxalacetic acids have important places in the cycle The structural relation of oxalacetic and oxalic acid might give rise to speculations concerning a possible physiologic relation At the present time, however, there is no available evidence that oxalic acid is concerned in the intermediary metabolism of the citric acid cycle or is connected in any manner with the formation or breakdown of oxalacetic acid in cellular metabolism

Blood oxalate levels are reported as elevated under the influence of adrenalin,^{167, 164} thyroxine¹⁶⁴ and anoxemia¹⁶⁶. The administration of insulin^{58, 145, 164} and thyroidectomy,¹⁶⁴ on the other hand, cause a fall. Urinary oxalate is elevated on exposure to hydrocyanic acid¹⁶⁶ and after exercise.¹⁶⁷ Dinitrophenol¹⁶⁶ and quinine¹⁶⁶ cause a fall in urinary oxalate.

Fate of Oxalates

The confusion centered around this aspect of the subject is enormous, and will not be clarified until a satisfactory method for the accurate determination of small quantities has been developed. The perplexity of the problem at the present time can best be demonstrated by enumerating some of the theories^{132, 136, 143, 155, 156, 168-170} that have been suggested. Oxalic acid is oxidized in the body, it is resistant to further breakdown, all organs are able to metabolize oxalic acid, blood forms and decomposes oxalic acid, skeletal muscle oxidizes oxalic acid but liver does not, oxalic acid is formed in the liver and skeletal muscle, liver cells destroy it, liver cells excrete it into the bile, oxalic acid is a source of carbon monoxide in the body, it is formed at the expense of uric acid, it is transformed into carbonate, it is changed into formic acid, and it is formed under conditions of reduced tissue metabolism.

There is no doubt that oxalates are excreted by the gastrointestinal tract and the kidney and appear in the urine, and there is some evidence that they also may be excreted in the bile. Their persistence in the urine during starvation suggests that to a certain extent they are endogenous in origin, but this problem as well as that of their subsequent fate requires further investigation.

ANTICOAGULANT ACTIVITY OF OXALIC ACID AND CERTAIN PLANT EXTRACTS

In 1939, Steinberg and Brown¹⁸⁶ reported briefly that extracts of certain plants decreased the coagulation time of rabbit's blood. Among the potent sources of these extracts were shepherd's purse, wood sorrel, beets, oxalis, citrus fruits, rhubarb and euphorbia. Attempts to determine the active principle resulted in the isolation of a colorless, crystalline material that they identified as oxalic acid. Of the various extracts, that from shepherd's purse apparently is best known. Copley and Lalich¹⁷¹ state that it is a common North American and European weed that in the past was used internally, as well as locally, to control hemorrhage. The report that oxalic acid administered parenterally accelerated coagulation of blood was rather startling in view of its well known anticoagulant activity *in vitro*. Nevertheless, it was used in the treatment of a large number of patients with a variety of hemorrhagic tendencies, as well as prophylactically to prevent postoperative bleeding. Steinberg et al.¹²⁸

reported more fully on their work in 1940 and concluded that the normal blood oxalate values range between 5.0 and 7.5 mg per 100 cc., that the coagulation time of blood varies inversely with its oxalic acid content, that the intravenous administration of oxalic acid causes a rise in blood oxalate greater than can be accounted for by the quantity of oxalate injected, that the intravenous injection of oxalic acid causes a decrease in coagulation time and that the administration of parenteral oxalic acid to several thousand patients with various types of hemorrhage gave a high incidence of gratifying results. It is important to note that their oxalate determinations were made by a modification of Suzuki's method, a procedure recently criticized by Barrett¹³⁰ and that their coagulation times were determined by the capillary-tube method, which is of questionable reliability.

Schumann¹⁷² reported the use of Koagamin, of which the active principles are oxalic and malonic acid, in a variety of obstetric and gynecologic hemorrhagic episodes with satisfactory clinical results, but his published studies are inadequate and the results are not convincing. Milliken,¹⁷³ in the same year, reported the successful use of Koagamin in the prevention of postoperative hemorrhage in prostatic surgery. He stated that the coagulation time was reduced by half, but failed to note the method used and gave no protocols. Martin¹⁷⁴ reported that intravenous oxalic acid reduced the clotting time of vitamin K-deficient chicks almost to normal and decreased the prothrombin time. In rabbits, he found that doses between 0.5 and 30.0 mg per kilogram of body weight caused a reduction in clotting time, whereas toxic doses of 100 mg per kilogram caused a prolongation. The clotting time in heparinized rabbits was unaffected. Page,¹⁷⁵ using the Lee-White method for the determination of clotting time, reported transient reductions to the upper limits of normal in three hemophiliacs after the intravenous injection of oxalic acid. One patient, however, failed to respond to a second administration. Blain and Campbell¹⁷⁶ reported experiments on rabbits and on 440 operative cases involving a wide variety of surgical procedures and claimed that the clinical results were excellent. Likewise, Herbst and Weinstein,¹⁷⁷ using Koagamin on 15 normal cases and 12 operative cases, concluded that a significant decrease occurred in bleeding time and coagulation time. The methods used (Duke method and capillary-tube method), however, are not the most reliable ones. Hulse¹⁷⁸ discussed the subject briefly, stated that oxalic acid definitely decreased blood clotting time and increased blood viscosity and was antagonistic to heparin and hirudin and recommended its use clinically. He presented no laboratory verification for his statements. A number of investigations that fail to confirm the value of oxalic acid, although quite limited, appear to warrant attention. Foster,¹⁷⁹ employ-

ing doses of oxalic acid comparable to those suggested for clinical use, was unable, employing a modification of the Howell method, to demonstrate any effect on the clotting time in normal rabbits, heparinized rabbits or vitamin K-deficient chicks. With large doses in rabbits he obtained a great prolongation of clotting time. Johnson,¹⁸⁰ using both oxalic acid and Koagamin, obtained no effects whatsoever on the coagulation time of 5 hemophiliacs. Copley and Lalich¹⁷¹ studied 2 cases of hemophilia with respect to bleeding time, clotting time and clot resistance after combined treatment with blood transfusions and an extract of shepherd's purse. All the bleeding times were normal. The clotting was decreased on one occasion only, and this followed the administration of both blood and extract. Clot resistance tended to be increased with the combined therapy. They raised the question of a phytothrombin in certain plant extracts.

In view of the fact that Koagamin is available for use, it is regrettable that most of the published experiments are based on the use of hematologic methods that are not the most reliable ones. At the present time it must be concluded that the use of oxalic acid or other dicarboxylic acids or plant extracts rich in oxalates for the treatment of bleeding disease is controversial, and that its exact value as a therapeutic measure requires further study.

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NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-FOURTH ANNIVERSARY

House of Delegates, May 14 and 15, 1945

THE House of Delegates convened at the Hotel Carpenter, Manchester, on May 14, 1945, at 7 30 p m, with Speaker Ralph W Tuttle presiding. The following members answered the roll call

The President, *ex-officio*
 The Secretary-Treasurer, *ex-officio*
 Richard W Robinson, Laconia
 Francis J C Dube, Center Ossipee
 W J Paul Dye, Wolfeboro
 Walter H Lacey, Keene
 Walter F Taylor, Keene
 Arthur B Sharples, Groveton
 Ralph N Jones, Whitefield
 Leslie K Sycamore, Hanover
 Howard N Kingsford, Hanover
 Israel A Dinerman, Canaan
 George F Dwinell, Manchester
 Donald M Clark, Peterborough
 Sullman G Davis, Nashua
 Robert E Biron, Manchester
 Mildred Chamberlin, Concord
 William P Clough, Jr, New London
 Gerard Gaudreault, Concord
 Willard C Montgomery, Epping
 Harry B Carpenter, Portsmouth
 Robert W Tower, Plaistow
 George G McGregor, Durham
 Francis H Nolin (alternate for Donald C Moriarty, Newport)
 B Read Lewin, Claremont

The Speaker declared a quorum present. On motion duly made and seconded, it was voted to omit the reading of the previous minutes, because of the publication of the proceedings.

The Speaker appointed the Credentials Committee as follows: Drs Clough, Jr, Biron and Dube

To the Committee on Officers' Reports, he appointed Drs Robinson, Chamberlin and Lewin. To the Committee on Communications and Memorials, he appointed Drs Davis, Handy and Dinerman. To the Committee on Nominations, he appointed Drs Clark, Dye, Tower, Moriarty and Sharples. For the Committee on Credentials, Dr Clough, Jr, reported that the credentials were in order.

The Secretary-Treasurer, Dr Carleton R Metcalf, presented his report, as follows:

MEMBERSHIP, DECEMBER 31, 1944

PAID	
Belknap County	26
Carroll County	13
Cheshire County	21
Coos County	25
Grafton County	57
Hillsborough County	98
Merrimack County	54
Rockingham County	49
Strafford County	29
Sullivan County	13
Not in County Society	3
	388
UNPAID	
Affiliate members	23
Honorary members	6
Members in service	129
	158
	546

The total membership on December 31, 1943, was 535

FINANCIAL STATEMENT

RECEIPTS

January 1, 1944 — balance forward	\$268 42
Belknap County	156 00
Carroll County	60 00
Cheshire County	108 00
Coos County	127 00
Grafton County	372 00
Hillsborough County	618 00
Merrimack County	324 00
Rockingham County	312 00
Strafford County	174 00
Sullivan County	84 00
Net receipts, 1944 annual meeting	95 02
Cash received at annual meeting	56 00
Members not in county societies	18 00
Refund (Cancer Committee)	6 60
Bond cashed (Women's Auxiliary)	74 00
Women's Auxiliary	87 25
Donations to National Physicians' Committee	191 00
Full subscription to <i>New England Journal of Medicine</i>	3 00
Trustees	500 00
Blue Shield (Coos County)	100 00
	<hr/>
	\$3734 29

EXPENDITURES

<i>New England Journal of Medicine</i>	
Journals	\$489 10
Full subscription	3 00
Cuts	6 19
Tables	10 06
Carleton R. Metcalf	
Salary	500 00
Reimbursement for room at annual meeting	4 20
Printing	64 25
Envelopes and stamps	40 59
Eagle and Phoenix Hotel Company (committee lunches)	65 85
Halftone cuts	40 02
Clerical work	150 00
Telephone and telegraph calls	58 81
Retaining fee	100 00
Guest speakers (fees)	22 20
Cancer Committee	50 00
Deering G. Smith	
Expenses at American Medical Association meeting	189 60
Procurement and Assignment	259 85
Dues collected at annual meeting	56 00
Benevolence Fund	
Women's Auxiliary	141 25
\$1 00 per each paid member	343 00
National Physicians' Committee (donations)	
Belknap County	25 00
Coos County	25 00
Sullivan	14 00
Strafford	1 00
Merrimack County	50 00
Rockingham County	48 00
Madeline A. May (stenographer at annual meeting)	147 51
Blue Shield (Coos County)	100 00
Mechanics Bank (service charges)	2 77
Trustees	
Incidentals	1 62
Accounting service	10 00
Refund on dues	13 00
Newspaper service (Blue Cross)	25 00
	<hr/>
	\$3056 87
Balance, January 1, 1945	677 42
	<hr/>
	\$3734 29

The total membership on December 31, 1944, was 546. This is an increase of eleven over the preceding year. Louis W. Flanders of Dover, who was elected president of the Society in June, 1924, has recently died. Frederic P. Scribner, of Manchester, for many years a valuable member

of the Committee on Scientific Work, died on July 17, 1944.

At the request of the Trustees, the Benevolence Fund has been turned over to that body. For several years heretofore, while the Trustees have been the official custodians, the accumulation of this fund had been entrusted to the Secretary-Treasurer. In last year's report I stated "This fund is to accumulate until it reaches \$10,000. The interest from the fund may then be used to help needy members of the Society." This statement was incorrect, there are several hundred dollars in the Benevolence Fund that are now available. I misinterpreted Chapter 11, Section 3, of our by-laws, which reads as follows:

When the total sum of the Benevolence Fund reaches ten thousand dollars (\$10,000) the House of Delegates may increase or decrease the yearly allotment from the dues of each member to the fund, and it shall also decide whether the income from the general fund shall continue as a source of revenue to the Benevolence Fund.

It should be noted that the allotment from the dues may be changed when the total sum reaches \$10,000. This statement implies, I suppose, that the allotment may not be changed before that time. As a matter of fact, two changes have been made, although the total sum has not yet been reached. A few years ago the amount of the annual assessment was doubled, and last year the House of Delegates voted to discontinue for one year further contributions to this fund from the annual dues. Such a vote was apparently not valid.

The proper course a year ago would have been to propose an amendment to this section of the by-laws at the first session of the House of Delegates and to vote on it at the second session, but if the intention of the House of Delegates has not been properly carried out and the customary contribution is made to the Benevolence Fund for the past year, it will merely mean robbing Peter to pay Paul, for we shall have to transfer money from the General Fund to the Benevolence Fund.

I suggest that Chapter 11, Section 3, be referred to the Committee on Amendments to the Constitution and By-laws, with the recommendation that it be modified or eliminated. If a change is voted it might be possible to make it retroactive for one year, so that the intention of the House of Delegates a year ago may be carried out. We must also decide about an assessment for the coming year.

While no money was added to the Benevolence Fund from the annual dues last year, we did receive donations from the following auxiliaries:

Hillsborough	\$18 75
Merrimack	20 00
Strafford	48 50

A bond received from the State Auxiliary in 1943 was cashed, and the further sum of \$74 00 was added to the fund in 1944.

In accordance with your instructions, \$50 00 was given to the Cancer Committee for its work.

I asked each county society to have its members contribute \$1 00 apiece to the National Physicians' Committee. During 1944, \$191 00 was received from the several counties, as follows:

Belknap	\$25 00
Coos	25 00
Merrimack	50 00
Rockingham	48 00
Sullivan	14 00
Strafford	29 00

In addition, the Hillsborough County Medical Society contributed \$51 00, which was sent directly to the National Physicians' Committee.

A report on the New Hampshire Physician Service, or Blue Shield, which was inaugurated and sponsored by the House of Delegates, will be given by its president, Leslie K. Svacumore. A further report will be given by the Executive Secretary at the general meeting.

There has been no vital legislation in the General Court during its recent session. I was on hand at five or six committee meetings, usually as an onlooker but, at the request of the State Board of Health, I spoke briefly on three occa-

sions as an individual, not as a representative of the New Hampshire Medical Society. The bills that were under discussion were

A bill to transfer certain health work now done by the Labor Department to the Department on Public Health. The bill was approved by the Committee on Public Health of the Society.

A bill to eliminate the doctor of medicine from the Board of Optometry, thereby placing five optometrists on the board instead of four optometrists and a physician.

A bill to liberalize the use and the coloring of oleomargarine.

A bill to enrich flour and bread by the addition of the vitamins that are initially removed in the process of milling.

A bill to require that employees of restaurants and other eating places obtain a medical certificate annually stating that they are free from tuberculosis and venereal diseases.

An increased fee is now being allotted to physicians for the obstetric care of the wives of servicemen. Beginning September 28, 1944, this fee was raised to \$50.00.

During the past year or two I have heard a statement made several times that the Society was being run by the "Old Guard." There is considerable truth in this statement, and I suggest that the Committee on Nominations scan the committee lists this year. While it may be desirable, because of their experience, to have members of the "Old Guard" in some of the key positions, it is likewise desirable to give younger men committee appointments so that they themselves will be familiar with the work of the Society when, a few years from now, they themselves become elder statesmen.

Of course, a good many of our younger men are in the armed services, but if it seems desirable, the Committee on Nominations ought to be able to make a start in the direction that I have suggested.

A modified Wagner Bill is in the making at Washington. I am told that it is the same old bill, the leopard has not changed his spots. Our two senators and our two congressmen are opposed to it. So far as I can find out, the doctors in the armed services are generally opposed to it and are fearful that something may be put over on them while they are absent.

Another group of planners in Washington is working out a new proposal for government-sponsored medical care.

The post-war project is being drafted by the United States Public Health Service and the Department of Agriculture's Postwar Planning Committee. It would spur a hospital building program such as the Nation has never seen. It would send thousands of doctors, dentists and nurses into rural areas and other places with little service, and it would provide compulsory health insurance.

The sponsors of the plan contend that there are many untended sick people in this country. They claim that in one third of the Nation's counties there is no hospital of any type and that thirty-three rural counties had no doctors at all even before physicians were called into the armed forces. They claim that another two hundred and forty-one counties had only one doctor for every two thousand people. The planners claim that the trouble is economic—that doctors go where there are concentrations of high-fee patients, and that the only solution is for the Government to step in.

Surgeon General Thomas Parran, head of the Public Health Service, declares, "The financing of a program for the total health care of the population must come through some system of prepayment, probably on an insurance basis, through public taxes or, perhaps, through a combination of both." Applied to the Nation, estimates indicate the cash involved each year in such a compulsory health scheme would be about \$1,800,000,000. A doctor operating under this federal plan would be given his choice of three different methods of obtaining his income.

In addition to this health program, the plan calls for special new centers to administer and practice public health. Each metropolitan area would have one or more base hospitals, from which there would radiate a series of rural hospitals more limited in service. There is also planned a program of health centers, which would be field stations of the future system of public health and medical care. Mobile clinics are also proposed.

Senate Bill 191 is much more modest. It provides for hospitals and health centers under state supervision but does

not regiment the doctors. This bill is sponsored by the American Hospital Association.

What are the members of the Society going to do if the Wagner Bill or some similar bill becomes law? Are we going to refuse to sign on the dotted line and try to practice medicine as we have heretofore practiced it, or are we going to become government doctors? Are we going to exhibit inertia, which is sometimes a property of mind as well as of matter?

We ought, individually, to give thought to this matter now. We ought to realize that changes in the method of practice are bound to come and that we ought to have a constructive hand in shaping such changes. We ought to take time by the forelock. Probably the best course is to accept wholeheartedly the leadership of the American Medical Association. We ought, at any rate, to hang together, for, as a wise old philosopher once said, "We must all hang together, or assuredly we shall all hang separately."

The Secretary-Treasurer then presented a letter from Elmer V. Andrews, Commissioner of the Department of Public Welfare, reading as follows:

At the spring meeting of the Medical Advisory Committee of Ophthalmologists, which was held May 2, 1945, at the Eagle Hotel, Concord, the committee voted to invite Thomas F. Reid, M.D., of Dover, to become a member of this committee.

In order that the records may be kept up to date and the Society may be kept informed on all departmental matters relating to the medical care field, I am writing to request that the House of Delegates approve Dr. Reid's acceptance of an appointment to this committee.

Dr. Metcalf explained that Dr. Reid was to meet with this committee three or four times a year, and consult with them as to the care of the eyes. In this way, the Society would be giving its sanction for the ophthalmologists on the committee. He requested that the Speaker entertain a motion to approve Dr. Reid's appointment. Such a motion was made by Dr. Dye, and was duly seconded and was carried.

Dr. Metcalf then outlined a letter from Helen Hinman, nutrition consultant in the State Board of Health. She wished to have a committee to help her in the nutrition of the children of the State. She had selected three men, who had agreed to serve in an advisory capacity. These men were Drs. Colin C. Stewart, of Hanover, Brockway D. Roberts, of Durham (chairman), and Simon Stone, of Manchester. On Dr. Metcalf's suggestion, it was moved and seconded that they be appointed as a Committee on Consultation in Nutrition.

Dr. Robinson, speaking on the motion, said that although he had no objection to the appointment, he objected to the precedent it would establish of permitting persons outside the Society to dictate or determine one of its committees. Dr. Metcalf replied that he had dictated the committee to a certain extent, since he had asked Miss Hinman to give him the names of the men she wanted, promising to submit them to the House of Delegates. She apparently wanted to have people who were familiar with nutrition, were interested in it, and would be willing to serve. Dr. Robinson then withdrew his objection, and the motion was duly carried.

Dr Metcalf next presented a financial report from Trustees for January 1, 1943, to December 31, 1944, as follows

RECEIPTS

Interest on various deposits	\$782 12
Interest on United States Bonds, Series G, other than those in the Benevolence Fund	456 25
Contributions to the Benevolence Fund	913 25
Total	\$2,151 62

EXPENDITURES

Expenses of the Society as voted	\$1,859 66
Prizes	150 00
Total	\$2,009 66

DEPOSITS

General Fund	
New Hampshire Savings Bank	\$3,152 98
Portsmouth Trust & Guarantee Company	1,223 90
Nashua Trust Company	398 23
United States Defense Bonds, Series G	3,000 00
Total	\$7,775 11

Artlett Fund	
Portsmouth Savings Bank (\$352.11 of this is a permanent fund, the income to be expended only for the benefit of medical science, as may be directed by vote of this Society)	2,998 92
United States Defense Bonds, Series G	2,000 00
Total	\$4,998 92

Ray Fund	
Strafford Savings Bank (\$1000.00 of this is a permanent fund, the income to be expended only for prize essays)	291 08
United States Defense Bonds, Series G	1,000 00
Total	\$1,291 08

Burnham Fund	
New Hampshire Savings Bank (\$1,140.00 of this is a permanent fund, the income to be expended only for prize essays)	1,064 01
United States Defense Bonds, Series G	1,000 00
Total	\$2,064 01

Benevolence Fund	
New Hampshire Savings Bank (\$688.87 of this is accrued income available for the purposes of the fund)	3,239 81
United States Defense Bonds, Series G	3,000 00
Total	\$6,239 81

Dr Robinson moved the acceptance of this report, and the motion was duly seconded and was carried

Dr Robinson for the Committee on Officers' Reports then spoke as follows

This Committee believes that it voices the general opinion of the members of our society in expressing respect for the diligent efforts and gratification for the accomplishments of the Secretary-Treasurer. We note with sorrow the deaths of two former officers of this society. We move the approval of this portion of our report

This motion was duly seconded and was carried

Dr Robinson then spoke as follows

Regarding the predicament that has arisen from alterations in the allocation of dues to the Benevolence Fund, we suggest that the Benevolence Fund return to the General Fund the amount it has received in excess of that designated in the by-laws after deducting the amount of the assessment that it should have received last year, had not such assessment been illegally withheld. We likewise suggest that the by-laws be amended to permit suspension of such assessments by unanimous vote of the House of Delegates at a regular meeting for the period of one year. To accomplish this, we move that Chapter XI, Section 3, of the by-laws be amended to read as follows

When the total sum of the Benevolence Fund reaches ten thousand dollars (\$10,000), the House of Delegates may increase or decrease the yearly allotment from the dues of each member to the fund, and it shall also decide whether the income from the General Fund shall continue as a source of revenue to the Benevolence Fund, except that at the time of any regular meeting of the House of Delegates, the yearly allotment may be abolished, increased or reduced, for a period of one year only, by unanimous vote of the members assembled

We move the adoption of this portion of our report, and that the proposed amendment to the by-laws be turned over to the Committee on Amendments to the Constitution and By-laws

The reason we make the suggestion that the Benevolence Fund return to the General Fund the amount it has received and take out money that should have been assessed last year is that we see no way of taking retroactive care of the fund

The Speaker asked whether this proposal should not be made on Amendments to the Constitution and By-laws. Dr Robinson said that it had been recommended to that committee

Dr Wilkins said that the original purpose was to build up a fund of \$10,000. The fund was started in 1932, and since there was at one time plenty of money, the rate was increased from 50 cents per member to \$1.00. Last year, the assessment was entirely suspended, because of the decrease of funds due to members' being in the Service. He added that he had no objection to the proposed amendment, but that it would simply slow up the reaching of the final goal

Dr Robinson expressed his willingness to yield any proposal to the Committee on Amendments to the Constitution and By-laws, but said he did not believe that a by-law could be abolished or suspended and then legalized a year later. He added that the by-law must be changed as of a particular time, and that it could not be changed as of last year now

Dr Kingsford thought that the Trustees intended the Benevolence Fund to be allowed to reach \$10,000, and then to be used in whatever way the House of Delegates desired. As he understood it, if the new motion went through, money could occasionally be taken out of the fund before it got to be \$10,000

Dr Dye asked whether the General Fund would have been faced with a deficit if the assessment had not been suspended last year. Dr Metcalf answered in the affirmative

Dr Dube suggested simply increasing the dues Dr Robinson then spoke as follows

As I understand it, several years ago, contrary to the by-laws, an allotment to the Benevolence Fund was increased. Last year, it was voted not to allocate the fund at all. Whatever is done must take care of the two circumstances. The best procedure, it seems to me, is to devise a simple arrangement of bookkeeping that requires no amendment, and to pass a simple amendment permitting the House of Delegates, by unanimous vote, to set the assessment aside for one year. This could be repeated as often as desired, and increased or decreased on the same basis. It is easy to refer this matter to the Committee on Amendments to the Constitution and By-laws, but it does not take care of the past changes and allocations.

The speaker pointed out that the by-laws could not be changed at one session and that any amendment proposed would have to be laid on the table until the following morning's meeting. He then put the original motion to vote, and it was carried.

Dr Robinson for the Committee on Officers' Reports said that it approved the policy of transfusing the offices and committees with new and younger blood, so that more of the members would be able to derive the benefits of service performed to the Society. It did not believe that new blood, properly typed, was so apt to cause reactions as would repeated usage of blood from the same donors. He moved the acceptance of this portion of the report, and the motion was duly seconded and was carried.

Dr Robinson then spoke on the questions propounded in the Secretary's report respecting individual attitudes to proposed federal legislation concerning the distribution of medical care. He said that various aspects of this subject had been touched on in the report of the delegate to the American Medical Association and in the report of the Committee on Medical Economics. It was the committee's best judgment that physicians should make up their minds that they will have no part in any plan that in one iota reduces the freedom of American medicine, but should hold themselves ready to co-operate constructively toward possible plans of the future that may promise better distribution of adequate medical care, provided they can be freed of this and other important evils. As Dr Metcalf had said, the Society could do no better than to follow the lead of the American Medical Association in these matters. He moved the acceptance of this portion of the report, and the motion was duly seconded and carried.

Dr Lawrence then spoke as follows

The House of Delegates of the American Medical Association is made up exactly like the Society's House of Delegates. The delegates to the former come from the various states, and those to the latter from the counties. After all, the county is the autonomous body, and not the American Medical Association or the state association. So that ideas of this kind, with regard to program or planning, can really best originate in the autonomous body and can be passed on from there. Inasmuch as we, as autonomous bodies,

are represented by delegates elected by them, those delegates should be instructed. In other words, it is one thing to say that we take the leadership of an organization that we think is, in a sense, other than ourselves, and another thing to take a leadership in which we take an active part in regard to the future of medicine at the present time. It seems to me that the future is best going to be served when every one of us takes his part in planning for the future and not asking someone to do it for him.

Dr Dye then presented the following report.

Report of the Committee on Amendments to the Constitution and By-laws

The majority of so-called "affiliate" members of the New Hampshire Medical Society are those physicians who have been members of this society for a continuous term of fifteen years and are either not less than sixty-five years of age or totally disabled, and who have been given such membership classification at the request of their county societies by a majority vote of the House of Delegates. Largely for this reason, many physicians throughout the State and the Merrimac County Medical Society, by direct unanimous vote, have suggested that the term "affiliate" shall be changed to the term "life," throughout the constitution and by-laws. This committee therefore recommends that the following changes be made in the constitution and by-laws:

The Constitution

Article 4, Section 1 This society shall consist of members, life members and honorary members.

Article 4, Section 3 Life members shall be those members whose dues are remitted.

The By-laws

Chapter 1, Section 5 Any physician who has been a member of this society for a continuous term of fifteen years, and is either not less than sixty-five years of age or totally disabled, on the request of his county society may be made a life member on a majority vote of the House of Delegates. Life members shall have the same rights and privileges as other members of the Society, but shall not be required to pay dues.

Chapter 3, Section 1 The general meetings shall include all registered members, life members, honorary members and guests, who shall have equal rights to participate in the proceedings and discussions, and, except guests and honorary members, to vote on pending questions. Each general meeting shall be presided over by the president, or in his absence or disability, or by his request, by the vice-president. Before it, at such time and place as may have been arranged, shall be delivered the annual address of the president and the annual oration, and the entire time of the session so far as may be shall be devoted to papers and discussions relating to scientific medicine.

W J PAUL DYE, Chairman
FREDERICK S GRAY
RALPH N JONES

Dr Robinson said that the Committee on Officers' Reports approved the changes as outlined in the report of the committee, and moved that the constitution and by-laws be so altered, subject to constitutional procedure. The Speaker directed that the matter be postponed until the morning meeting.

Dr Amsden then presented the following report

Report of the Necrologist

NAME	ADDRESS	DATE OF DEATH
Bergeron, Pierre	Manchester	May 7, 1944
Flanders, Louis W	Dover	January 16, 1945
Grimes, Warren P	Hillsborough	November 13, 1944

awkins, Frederick L	Meredith	November 8, 1944
ndman, Elbert A	Plaistow	October 18, 1944
rmandin, Armand	Laconia	February 14, 1945
er, Charles F	Manchester	January 29, 1945
rgent, Frank H	Pittsfield	July 11, 1944
nbner, Frederick P	Manchester	July 17, 1944

HENRY H AMSDEN, *Necrologist*

Dr Robinson for the Committee on Officers' reports recommends the acceptance of this report, and in recognition of the service given by the departed members to the Society, suggested that the House rise and honor their names with a minute of silence. This was done.

Dr Stewart then presented the following report

Report of the Committee on Child Health

War conditions have again precluded much activity on the part of this committee. We expect shortly to send out a letter summarizing the most recent views on prophylaxis against the infectious diseases of childhood. This would include the use of gamma globulin as protection against measles, this material having recently become available through the State Department of Health.

Safeguarding the health of children in foster homes is another subject that has been considered. Protection against possible exposure to tuberculosis, along the lines discussed with Dr Kerr, has been urged.

We have reviewed adoption practices in New Hampshire. Many doctors do not know the aids available to them in this field, and we have co-operated with the Children's Aid Society in the preparation of literature designed to bring this information to them. Your chairman appeared at a legislative hearing relative to proposed changes in the law concerning adoption.

COLIN C STEWART, *Chairman*
B READ LEWIN
FRANKLIN ROGERS

Dr Robinson for the Committee on Officers' Reports approved the report and moved its acceptance. The motion was duly seconded and carried.

Dr Wilkins then presented the following report

Report of the Committee on the Control of Cancer

Two years ago the State Executive Committee of the Field Army of the American Cancer Society offered financial aid to physicians connected with the state cancer clinics for refresher courses at various cancer centers in New York City and Boston. Only six physicians have availed themselves of this privilege, but each of these has expressed deep appreciation of the clinical privileges afforded him in these centers. It is now suggested that plans be made during the coming year for one or two days' intensive instruction in the diagnosis and treatment of cancer, the course to be open to general practitioners as well as to those especially interested in cancer treatment. These plans will be elaborated further and communications regarding them will be sent to every member of the Society. It is anticipated that the expenses of attending this course will be borne by the Field Army of the American Cancer Society. The Executive Committee of the Field Army would like the approval of this society for this plan.

The Field Army has conducted its usual drive for members during April, and it is to be noted that the change in name from "Women's Field Army" to "Field Army" was made in order to encourage the enlistment of men as well as women interested in cancer control. The Field Army has continued its program of lay education and preparation of dressings for indigent cancer patients, and has provided transportation for patients to clinics and hospitals. This year educational material for cancer educa-

tion has been furnished the high-school science classes in both public and parochial schools in Manchester, and it is to be hoped that such instruction will be introduced into the high schools of all communities in the State.

The New Hampshire Cancer Commission clinics have functioned as usual. The total number of visits to the clinics was 1582. Of these, 705 were made by new patients and 877 were return visits. Of the new patients, 61 per cent had cancer, this percentage having gradually risen from 36 per cent in 1934. During the last fiscal year the Commission paid for 4338 hospital days for patients unable to finance their own hospital expenses. In comparison with most other states, New Hampshire is fortunate in the facilities for cancer diagnosis and treatment made available by the Cancer Commission.

Your committee has sent three communications to all physicians within the State. The first was a pamphlet containing two articles, "The Doctor's Responsibility" and "The Office Detection of Cancer." Under both these subjects were discussed points that had been stressed before in previous letters, all of them important in relation to cancer diagnosis. The second was a letter explaining the difference between carcinoma simplex and adenocarcinoma, about which there had been confusion in the minds of some physicians after receiving pathological reports of tumors or biopsies. It stated that carcinoma simplex is usually more malignant and more invasive than adenocarcinoma and metastasizes more rapidly. The third was a letter reiterating the need of not overlooking the importance of any abnormal rectal or vaginal bleeding, the necessity of recognizing the fact that such bleeding is usually due to pathologic change and the need for investigation until the cause is discovered. Mention was also made that after the menopause, estrogenic therapy may cause flowing similar to that resulting from adenocarcinoma of the fundus. In rectal bleeding, physicians were reminded again of the proper sequence of methods to determine the cause, in the order named: digital examination, proctoscopy and x-ray examination — not the reverse.

Of the \$50.00 appropriated for the use of the committee, there was spent \$31.20 for stationery, postage and printing. A check for the balance of \$18.80 has been sent to the Treasurer, the large balance being due to fewer physicians on the mailing list. The committee requests \$40.00 for the ensuing year.

GEORGE C WILKINS, *Chairman*
RALPH E MILLER
GEORGE F DWINELL, *Secretary*

Dr Robinson for the Committee on Officers' Reports commended highly the diligent efforts of the Committee on the Control of Cancer, and said that the Committee was confident of a continuation of the same effort in the future. He recommended that the request for \$40.00 to carry on its activities be granted. The committee, he continued, took recognition of the fact that early diagnosis is the best present answer to a lower mortality from this disease, and wished to go on record as approving the suggested plan for intensive instruction in the diagnosis and treatment of cancer as outlined in the report. He moved its approval, and also moved that the State Executive Committee of the Field Army of the American Cancer Society be given notice of such action on the part of the House of Delegates. This motion was duly seconded and carried.

Dr Blood then presented the following report

Report of the Committee on Maternity and Infancy

This is the eleventh year of this study of maternal and infant deaths.

Maternal Mortality

There were 26 maternal deaths and 8695 live births, a maternal mortality rate of 2.99 per 1000 live births. This may be compared with the figures for 1943 of 24 maternal deaths and 9825 live births, a maternal mortality rate of 2.44 per 1000 live births. Over a period of ten years, the highest mortality was that of 1935, 6.1 per 1000 live births, with 45 deaths, the lowest was that of 1942, 1.6, with 15 deaths.

The 26 maternal deaths have been classified according to the *International List of Causes of Death*, as follows:

CLASSIFICATION	No of DEATHS
Puerperal toxemia (death after delivery)	9
Infection during childbirth and puerperium	7
Accidents of pregnancy (death before delivery) *	5
Inversion of uterus	2
Hemorrhage (1 before delivery and 1 after)	2
Ectopic gestation	1
Total	26

The committee has reclassified these for the purpose of this report in the following way:

CAUSE OF DEATH	
Accidents of pregnancy	11
Puerperal emboli	4
Anesthesia	2
Inversion of uterus (with hemorrhage)	2
Attempted abortion with poison	1
Cerebral embolus (before delivery, cause unknown)	1
Multiple pulmonary emboli due to meconium and amniotic fluid (before delivery)	1
Hemorrhage	2
Internal hemorrhage	1
Probable placenta previa (case seen only by coroner)	1
Toxemia (all types)	9
Puerperal sepsis	3
Ruptured ectopic pregnancy	1
Total	26

The committee has further classified these cases on the basis of data submitted in one of three groups: unavoidable, patient's fault and probably avoidable. There were reports on 5 deaths that gave insufficient data for classification. In 2 of these, one eclampsia and the other puerperal infection, no information was submitted. The other 3 deaths were recorded on the certificate as due to postpartum eclampsia, eclampsia and internal hemorrhage, respectively. The remaining 21 cases were classified as follows: unavoidable, 11; patient's fault, 6; avoidable, 4. Of the 11 deaths classified as unavoidable, 6 were due to embolism, 2 to inversion of the uterus, 2 to toxemia and 1 to ectopic gestation. Of the 6 deaths classified as the patient's fault, — that is, she failed to seek medical attention or failed to carry out medical advice, — 3 were due to toxemia and 1 to hemorrhage, probably placenta previa, in 1 case the actual cause of death was pneumonia following a normal delivery when the patient left the hospital against advice, and in 1 case death was due to poison from drinking oil of cedar in an attempt to abort. Of the 4 deaths classified as probably avoidable, 2 were due to anesthesia. The committee is of the opinion that, with the difficulty at the present in securing physicians to give anesthesia, the attending physician must assume the responsibility for it and be more careful and attentive to the procedure. There was 1 death due to toxemia that the committee thought might have been avoided had adequate treatment been given. One patient died of postoperative complications following a cesarean section. In this case some of the committee believed that the procedure of choice would have been to allow the patient to deliver normally.

All the deliveries took place in a hospital.

The deaths by county were as follows: Belknap, 1; Carroll, 1; Cheshire, 1; Grafton, 2; Hillsborough, 8; Merrimack, 2; Rockingham, 3; Strafford, 6; and Sullivan, 1. Coos County is the only one having no maternal deaths.

The committee has certain recommendations to make and these will appear later in detail in a printed report, copies of which will be sent to each member. Briefly the points are as follows:

The value of Rh-factor typing in obstetric patients and having facilities available for typing in hospital laboratories.

The value of autopsies, with an increasing effort on the part of physicians to obtain an autopsy.

The increased responsibility of the attending physician in giving patients in labor an anesthetic.

The treatment in toxemias. (There is evidence that physicians still fail to give adequate and proper treatment in toxemias. Toxemia is still highest on the list as a cause of maternal deaths. The treatment in toxemias cannot be overstressed.)

Infant Mortality

Included in this group are those infants who died under one year of age. There were 322 infant deaths in 1944, giving an infant death rate of 37.0 per 1000 live births, as compared with 420 deaths in 1943, a rate of 42.9. Prematurity as a single cause still accounts for the largest number of deaths.

Stillbirths

There were 232 stillbirths in 1944, as compared with 211 in 1943. The cause for the most part is reported as known.

ROBERT O. BLOOD, Chairman
BENJAMIN P. BURR
MARION FAIRFIELD

Dr. Robinson expressed the sincere recognition of the Committee on Officers' Reports of the invaluable service rendered to the welfare of the State by the Committee on Maternity and Infancy. He said it believed that this committee renders likewise an invaluable service to every conscientious physician practicing obstetrics, both in New Hampshire and throughout the civilized world. Such statistical reports, carefully analyzed, he continued, should serve as the most solid available foundation on which physicians can build for the betterment of methods of obstetric care. He therefore urged every member of the Society to give this committee his fullest co-operation as the occasion may arise, scientifically and without prejudice. He moved the acceptance of this report, and the motion was duly seconded and carried.

Dr. Sycamore then presented the following report:

Report of the Committee on Medical Economics

New Hampshire Physician Service. The past year has seen the fruition of the project toward which your committee had directed the major portion of its labors in the preceding three years, ably assisted by the officers of the Society and the House of Delegates. On August 1, 1944, the New Hampshire Physician Service issued its first contracts, and since then has proved to be a lusty offspring, on which this committee has kept a paternal eye, although, of course, with the completion of incorporation, control and authority passed to the hands of the Board of Trustees of the New Hampshire Physician Service. An account of the operations of the plan to date is given in the report of its president.

Your committee has noted with interest the endorsement of medical-service plans given by the American Medical Association and the National Physicians' Con-

mittee. At the annual meeting of the American Medical Association last June, the report of the Committee on Medical Service and Public Relations, later accepted by the House of Delegates, stated "All constituent state associations have been urged to develop voluntary plans [for medical expense insurance] within their territory. The American Medical Association will assist in the development, correlation and integration of such plans." It is evident, therefore, that the New Hampshire Medical Society, in constituting the New Hampshire Physician Service, has acted in accordance with the considered judgment of our national association.

National Physicians' Committee The National Physicians' Committee has directed its efforts in the past year first to conducting a public opinion poll that indicated a preference for voluntary sickness insurance over national compulsory insurance, and second, to promoting a campaign for the extension of such voluntary insurance of any type. Because some members of our society have expressed a certain degree of doubt as to the validity of the publicity and methods of the National Physicians' Committee, your committee recommends, as it did last year, that the question of financial support for this organization be left to each physician.

Association of American Physicians and Surgeons A new organization has entered the field of medical economics and public relations, originally organized under the above name by the Lake County (Indiana) Medical Society and now claiming membership in all states, with endorsement by several county societies. The main purpose of the association appears to be an unalterable antagonism to any form of a governmental national health program, using as a weapon a professional boycott against any such program and against any fellow physicians who might co-operate with the program. Your committee recognizes the right of physicians to so organize, however, it is our belief that it is not expedient to approve so completely a closed-minded attitude as this organization insists on, for reasons that we think will become evident in the discussion of national compulsory sickness insurance. We also find it difficult to justify on the basis of this organization's acknowledged activities, the annual dues of \$10.00 necessary to continuing membership therein.

National compulsory sickness insurance It is expected that a modified version of the Wagner-Murray-Dingell Bill will be introduced into the present Congress, undoubtedly incorporating some of the proposals advanced by the present Pepper Committee on Wartime Health and Education. Your committee believes that we should make no blanket condemnation before the fact, but should be prepared to make a careful evaluation of any such bill on its merits. We believe, furthermore, that governmental participation in the economic aspects of medical service may conceivably become expedient and desirable. There is merit, for example, in the regional organization of hospitals and health centers, with government assistance in providing the necessary facilities. Under such a plan the smaller diagnostic health centers and hospitals are integrated with progressively larger units so that necessary consulting and special services are readily available to all. A logical extension of such regional organization is the development of group practice around the hospitals. The medical profession, we believe, will contribute more to its own and the public welfare by indicating its readiness to confer with governmental agencies in an attempt to work out a mutually satisfactory solution than by assuming an uncompromising antagonism to any such attempt. We would point out that the existence in New Hampshire of a strong and widely inclusive voluntary prepaid-medical-care program under the auspices of the New Hampshire Medical Society would be a cogent argument, in any discussion, for the capability of the medical profession in our state to handle the professional aspects of medical care, and we therefore bespeak the vigorous support of all members of the Society for the New Hampshire Physicians Service.

L. K. STAMORE *Chairman*
FRANCIS J. C. DUBE
R. W. ROBINSON

Dr Robinson said that the Committee on Officers' Reports had no special comment to make on the above report. For himself and the members of his committee, he approved each part of it, except that he detected a feeling, not quite unanimous, that it indicated a little too much willingness to participate in plans of the federal government for socialized medicine. He was willing to defend the report, but had no other to make.

Dr Dube moved the acceptance of the report, and his motion was duly seconded and carried.

Dr Bowler then presented the following report

Report of the Committee on Medical Education and Hospitals

The activities of this committee during the past year have been extremely limited, owing to conditions at this time that have permitted no program of post-graduate study. The Commonwealth Fund fellowships have been discontinued for the duration of the war.

The Speakers' Bureau has been used by a few county societies, but this program has necessarily been restricted as well.

The New England Regional Committee of the Wartime Graduate Medical Program has continued in operation, and on it this committee has been represented. The services of several men in the Society have been utilized in connection with this program in lectures and demonstrations at various station hospitals in this region.

Quite recently a commission has been named by Governor Charles M. Dale for the survey of hospital facilities in New Hampshire. The appointment of this committee follows the outline of Senate Resolution No. 191, a bill providing for a national survey of hospitalization facilities, to be on a state basis. This commission is representative of various groups interested and concerned in the general problem of health and hospitalization and to it have been appointed Dr George C. Wilkins, of Manchester, and the chairman of this committee. It is entirely possible that out of this survey may develop more activities on the part of this committee.

JOHN P. BOWLER, *Chairman*
JAMES W. JAMESON
HERBERT L. TAYLOR

Dr Robinson moved the adoption of this report. The motion was duly seconded and carried.

Dr Powers then presented the following report

Report of the Committee on Public Health

This is the third anniversary of the Committee on Public Health. For the past year the Committee has consisted of Dr Anthony E. Peters, of Portsmouth, Dr Clinton R. Mullins, of Concord, and Dr Harris E. Powers, of Manchester, the latter serving as chairman. It has been the function of this committee to keep in touch with the public-health activities in our state, and to keep abreast of the functions of other public-health units in the scattered sections of the country. This has been accomplished by communications from the Committee on Public Health of the American Medical Association and by direct contact with the workers in our own community.

Again this past year our industries have been pressed hard in securing employees, owing to the urgency of the war demands. In many instances we have had to resort to older men, and men who are less well physically qualified for the arduous duties they have had to carry on. Both employer and employee have labored under extenuating circumstances, tension has been high, and with these facts

Maternal Mortality

There were 26 maternal deaths and 8695 live births, a maternal mortality rate of 2.99 per 1000 live births. This may be compared with the figures for 1943 of 24 maternal deaths and 9825 live births, a maternal mortality rate of 2.44 per 1000 live births. Over a period of ten years, the highest mortality was that of 1935, 6.1 per 1000 live births, with 45 deaths, the lowest was that of 1942, 1.6, with 15 deaths.

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FRANCIS J. C. DUBE
R. W. ROBINSON

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Dr. Dube moved the acceptance of the report, and his motion was duly seconded and carried.

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The Speakers' Bureau has been used by a few county societies, but this program has necessarily been restricted as well.

The New England Regional Committee of the Wartime Graduate Medical Program has continued in operation, and on it this committee has been represented. The services of several men in the Society have been utilized in connection with this program in lectures and demonstrations at various station hospitals in this region.

Quite recently a commission has been named by Governor Charles M. Dale for the survey of hospital facilities in New Hampshire. The appointment of this committee follows the outline of Senate Resolution No. 191, a bill providing for a national survey of hospitalization facilities, to be on a state basis. This commission is representative of various groups interested and concerned in the general problem of health and hospitalization and to it have been appointed Dr. George C. Wilkins, of Manchester, and the chairman of this committee. It is entirely possible that out of this survey may develop more activities on the part of this committee.

JOHN P. BOWLER, *Chairman*
JAMES W. JAMESON
HERBERT L. TAYLOR

Dr. Robinson moved the adoption of this report. The motion was duly seconded and carried.

Dr. Powers then presented the following report:

Report of the Committee on Public Health

This is the third anniversary of the Committee on Public Health. For the past year the Committee has consisted of Dr. Anthony E. Peters, of Portsmouth, Dr. Clinton R. Mullins, of Concord, and Dr. Harris E. Powers, of Manchester, the latter serving as chairman. It has been the function of this committee to keep in touch with the public-health activities in our state, and to keep abreast of the functions of other public-health units in the scattered sections of the country. This has been accomplished by communications from the Committee on Public Health of the American Medical Association and by direct contact with the workers in our own community.

Again this past year our industries have been pressed hard in securing employees, owing to the urgency of the war demands. In many instances we have had to resort to older men, and men who are less well physically qualified for the arduous duties they have had to carry on. Both employer and employee have labored under extenuating circumstances, tension has been high, and with these facts

in mind it is not unreasonable to presume that differences of opinion between labor and management might occur frequently. In our state, however, co-operation appears to have been excellent, and only minor instances have occurred to delay the war effort. Part of the credit for this is due to the progress of industrial health within the state boundaries. The State Board of Health, with a limited group of employees, has made repeated inspections of industrial sites and offered its assistance in maintaining the highest possible working standards. Its co-operation has been accepted, and in most instances the progress of industrial health in New Hampshire has been moving steadily forward. Our problems have not all been solved, but we are making progress.

As an illustration, the chairman of this committee had the privilege in August, 1944, of making a tour of inspection of the northern section of the State, together with Dr. Alfred Frechette, State Health Officer, and Captain Forrest Bumford, acting director of the Division of Industrial Hygiene. This trip was made primarily for the purpose of gaining firsthand knowledge of how the State Board of Health functions, especially in the field of industrial hygiene. The trip took us through the north country, where we inspected the Brown Manufacturing Company at Berlin. It was indeed a surprise to go over the holdings of this company and learn something of how the lumber industry functions. We followed the process from breakfast to supper, starting out with the men and watching their activities throughout the day. We had the opportunity of going through the quarters of the lumberjacks, inspecting the mess shacks and examining the refrigeration plants. Dr. Samuelson, who serves as the medical director of the company, acted as our guide and escorted us through several of the camp sites. He took us through the infirmary and advised us of the care the employees were given in both sickness and injury. In the pulp mills, where a large number of chemicals are used in the processing of lumber, I learned that injurious gases are constantly given off and that unless precautions are taken the health of the employees may be seriously impaired. I watched the study of such problems through chemical tests taken over a period of twenty-four hours under actual working conditions and was interested in the methods suggested by the State Board of Health for overcoming these hazards.

Complicated surveys of similar character are constantly being made by the State Board of Health to increase the efficiency of employees by improving sanitary conditions under which they work. One does not have to go back many years to find a time when such activities would have been considered extravagant and unnecessary, but the profession is fast becoming conscious of the necessity of preserving the health of labor and the safety of the citizens.

This brings up another extremely important problem that must sooner or later be faced, very little has been done in the resort sections of the State to ensure proper health standards among vacationists, and as the tourist trade grows and overnight camp and trailer sites increase in number, sanitary conditions about these areas are certainly going to demand more direct supervision.

The Society owes a debt of gratitude to the State Board of Health, which at the present time is functioning with a limited personnel and under somewhat trying circumstances owing to the lack of suitable housing facilities. The various departments are scattered among several buildings, and co-ordination under such an arrangement is difficult. Our moral support for suitable housing facilities for the State Board of Health as a unit will aid materially in obtaining such quarters and will improve the efficiency of the department. Public health is primarily a medical problem, and it is our duty as physicians to keep it that way.

It has been a pleasure and privilege to serve as your representatives on this committee for the past year.

HARRIS E. POWERS, *Chairman*
ANTHONY E. PETERS
CLINTON R. MULLINS

Dr. Robinson said that the Committee on Officers' Reports found much of interest in the report of the Committee on Public Health. It recommended

commendation of the State Board of Health of its efficient performances, especially in the cause of industrial hygiene, by the House of Delegates. The committee suggested that the House go on record as approving, when betterment of personnel makes it practicable, more rigid sanitary protection for the users of recreational facilities. He moved the acceptance of this portion of the report. This motion was duly seconded and carried.

Dr. Robinson likewise moved that the House of Delegates go on record as being in favor of more efficient housing of the State Board of Health than is now employed. He moved the acceptance of this portion of the report, and the motion was duly seconded and carried.

Dr. Smith then presented the following report:

Report of the Delegates to the House of Delegates, American Medical Association

The annual session of the House of Delegates of the American Medical Association was held at Chicago in June, 1944. It was well attended, especially by the doctors in the services. Your delegate served as chairman of the Reference Committee on Credentials. Emphasis throughout the meetings was on the war and subjects allied to it.

The Committee on Postwar Medical Service, appointed to assist veterans in location and post-graduate work, reported that questionnaires had been sent to all medical officers asking them what they wanted after the war as refresher courses, internships, residencies and so forth. Plans should be made to assist the veterans in obtaining this post-graduate work and in their relocation. Accordingly, it is recommended that this society establish a Committee on Postwar Medical Service, to work with the similar committee of the American Medical Association. The establishment of a loan fund by the Society, to be administered by this committee or by the trustees, or both, should be considered. Loans to returning medical officers may prove of material assistance in re-establishing themselves in their practice.

The general program of Emergency Maternal and Infant Care was approved, but the methods of payment were disapproved. It was recommended that the program be transferred from the Department of Labor to the Department of Public Health, and that full control and regulation of it be placed completely in the public-health department of each state.

The Council on Medical Service and Public Relations has established a Washington office. It has studied proposed legislation, voluntary insurance diagnostic clinics and medical-service bureaus, and has collected information and data concerning all aspects of medical care. Bulletins of the activities of the council have been sent to the county and state societies, and the information collected is available to all.

Dr. Kretschmer suggested that the family physician should take a more active part in the education of the public in social medical questions. "It would be well," he said, "if every member of the profession would make a personal effort to explain to patients, whenever the opportunity offers or can be made, the problems with which medicine is faced, and particularly the results of governmental dictation and supervision of medical practice."

New England was honored by the election of Roger I. Lee, of Boston, as president-elect of the Association. The 1945 session has been canceled, although it is expected that the House of Delegates will meet in Chicago in the fall. Extensive plans are in preparation for the one hundredth anniversary of the American Medical Association in 1947. It is hoped that either the war will be over or conditions will have so changed that a proper celebration may be held at Atlantic City.

An effort has been made in this report to bring to your attention some of the high lights of the meeting. The complete proceedings have been published as usual in the *Journal of the American Medical Association*.

DEERING G. SMITH

Dr Robinson for the Committee on Officers' Reports paid tribute to the ability and excellent service rendered to the state and national societies by Dr Smith. He moved the acceptance of this portion of the report, and the motion was duly seconded and carried.

Dr Robinson then spoke as follows:

Regarding the creation, on the part of the New Hampshire Medical Society, of a loan fund as an aid to the re-establishment within the State of physicians returning from service in the armed forces, we, of course, are in complete approval of the sentiment that fathers this idea, but believe that the size of such a fund as might be raised within our abilities would bear little practical significance when compared with the size of the service that it was fostered to perform, though its actual benefit would be small and that the potentialities toward the production of ill-feeling might be large.

We believe that it is intended that such funds be made available as a part of postwar nation-wide planning and, if not, that local banking facilities will be readily available to physicians for such purposes, as they have in the past.

We think that the Society should approve the appointment of a Committee on Postwar Medical Service to co-operate with the similar committee of the American Medical Association. We suggest that this committee be appointed by the chair, and not be elective. We recommend that it have a member from each county in the State, and that one of these be a member of the Committee on Medical Preparedness and another a member of the Committee on Medical Education and Hospitals. We believe, likewise, that each appointee should have the ratification of his own county society. We move the acceptance of this portion of our report.

This motion was duly seconded and carried.

Dr Robinson then said:

We approve the transference of the program of Emergency Maternal and Infant Care from the Department of Labor to the Department of Public Health, and the proposal that the full control and regulation of this plan in the State of New Hampshire shall remain completely in our own State Board of Health. We believe that the value of public education on social medical questions by individual physicians to their individual patients cannot be overemphasized, and recommend that the words of Dr Kretschmer, as quoted in our delegate's report, be read at the General Assembly. We move the acceptance of this portion of our report.

This motion was duly seconded and carried.

(To be concluded)

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 31341

PRESENTATION OF CASE

A forty-three-year-old woman entered the hospital complaining of dysphagia.

Six weeks before admission, while eating, she was seized with a sudden, severe lower substernal pain radiating to the right scapular region. For several days she felt generally miserable. The pain slowly subsided, but thereafter she found that ingestion of food brought on a similar attack, and she therefore did not partake of any solid food. She had no difficulty with fluids. There was no nausea or vomiting. The pain usually lasted one or two hours. On one occasion it persisted all night and the patient could not lie down.

She had had an attack of "pleurisy" four years

*On leave of absence

before entry and again three years later. One sister had died of pulmonary tuberculosis.

Physical examination revealed a well developed, well nourished woman in no acute distress. There was deafness in the left ear, and a diaphragm that seemed to be high on the right. The feet were cold and clammy, and the dorsalis pedis arteries were not palpable. Otherwise, the examination was negative.

The temperature was 99°F, the pulse 70, and the respirations 20. The blood pressure was 125 systolic, 85 diastolic.

Examination of the blood showed a white-cell count of 8200, with 69 per cent neutrophils, 23 per cent lymphocytes, 7 per cent monocytes and 1 per cent eosinophils, the hemoglobin was 13.6 gm. The nonprotein nitrogen was 30 mg. per 100 cc., the chloride 106 milliequiv. per liter, and the total protein 6.5 gm. per 100 cc. The urine gave a + test for albumin, and the sediment contained 5 white cells and a rare coarsely granular cast per high-power field.

An x-ray film taken outside the hospital showed a pressure defect 3.5 cm. in length in the barium-filled esophagus, this defect was anteriorly placed at the level of the carina. The normal mucosal pattern could be traced through it, and no ulcer was apparent. The mass caused no great obstruction to the passage of barium. The stomach and duodenum appeared normal in form and function.

On the seventh hospital day an operation was performed.

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(Fig 1) The only further comment that might be made is that there does not seem to be much swelling of the mucosa as it passes from the defect, nor does there seem to be rigidity of the wall—it is quite flexible. This large film quite well rules out a hiatus hernia.

DR SCHALL The x-ray films demonstrate that there is a normal esophageal wall. There is no infiltration of the wall, but there is an extrinsic mass. In this view here, the right and left main-stem bronchi are patent and there is no broadening of the carina. Therefore, from the x-ray films one can say that this patient had a mass involving the esophageal wall, and that brings up the possibility of a benign new growth of the esophagus. There is no mention in the history of the Hinton test.

DR. CASTLEMAN It was negative.

DR. SCHALL Gummas of the esophagus are rare. A sister had died of tuberculosis. I assume that there was no evidence of pulmonary tuberculosis in this patient. I do not believe that this was a tuberculoma. I am inclined to think that this was a benign tumor of the esophageal wall, perhaps a tumor arising from the muscle—a leiomyoma.

DR. S. A. THEODORE Could this have been a fibroma originating in the mediastinum?

DR. CASTLEMAN That is a possibility. We have also seen intramural neurofibromas of the esophagus.

DR. HELEN PITTMAN Perhaps it is one of the intramural extramucosal tumors of the esophagus that Dr. Schatzki used to talk about*.

CLINICAL DIAGNOSIS

Carcinoma of esophagus?

DR. SCHALL'S DIAGNOSIS

Benign tumor of esophageal wall (leiomyoma?)

ANATOMICAL DIAGNOSIS

Tuberculosis of mediastinal lymph nodes

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN Dr. Richard Sweet operated on this patient. He had a great deal of difficulty exposing the lesion because of dense fibrous adhesions over the lung. When he separated these, he found a calcified focus on the pleura, which he thought was due to old tuberculosis. When he pushed the lung aside and got to the region of the esophagus, it was obvious that the mass was composed of an aggregation of enlarged lymph nodes that was pressing on the esophagus. He was able to remove them without entering the esophagus. At the operation a frozen section of one of the lymph nodes showed active tuberculosis. The nodes were removed to free up the obstruction, but nothing further was attempted. The patient is doing well.

The sections showed microscopically the character-

istic caseation and Langhans giant cells of active tuberculosis. There apparently was no active tuberculosis in the lungs.

CASE 31342

PRESENTATION OF CASE

A five-day-old girl was admitted to the hospital because of vomiting since birth.

The infant was delivered with low forceps at term after a prolonged first stage of labor that lasted three days. The birth weight was 6 pounds, 2 ounces. She appeared normal at birth but began to vomit green material during the first night and continued to vomit at frequent intervals until admission. She passed normal meconium twice, then the stools became blue gray, and shortly before admission they became yellow. During the three days before admission the abdomen was markedly distended. She voided at least twice a day. The formula, which could not be retained, was supplemented by small subcutaneous clyses. Barium was given by mouth in the maternity hospital, but no abnormality was observed.

Physical examination revealed a slightly jaundiced, moderately dehydrated infant with a lusty cry, weighing 5 pounds, 12 ounces. The cranial sutures were over-riding, and the fontanelles were sunken. The abdomen was markedly distended, and peristalsis was practically absent. The cord was normal. The heart and lungs were normal. She vomited fecal material and passed by rectum small amounts of fluid with tiny particles of solid yellow stool.

The temperature was normal, the pulse 140, and the respirations 19.

Examination of the blood showed a red-cell count of 4,200,000, with 13.2 gm of hemoglobin. The cells and platelets appeared normal. The white-cell count was 6600, with 20 per cent neutrophils, 68 per cent lymphocytes and 12 per cent monocytes. The urine was normal. The blood was Rh negative.

An x-ray examination showed the abdomen to be distended. There appeared to be free air scattered throughout the peritoneal cavity. There were numerous small areas of calcification. There was opaque material in the stomach and in one loop of bowel.

The infant was promptly started on measures of hydration preparatory to operation, but she died before operation could be performed.

DIFFERENTIAL DIAGNOSIS

DR. ALLAN M. BUTLER We have an infant who began to vomit green material during the first day of life and continued to vomit at frequent intervals until admission, which, unfortunately, was not until five days later.

*Schatzki R., and Hawes L. E. Roentgenological appearance of extramucosal tumors of the esophagus. *Am J Roentgenol* 48:1-15, 1942.

DIFFERENTIAL DIAGNOSIS

DR LEROY A SCHALL The history of this case, although short, brings out several positive facts. First, there was severe substernal pain, which radiated to the right scapula, and then following the pain the patient had difficulty in swallowing. Whether this pain was due to obstruction or caused by eating is not brought out in the history. She had no difficulty with liquids. There was no apparent loss of weight on admission, nor had there been nausea or vomiting. There is no mention of regurgitation nor of belching, or of whether, if there was belching, this relieved the pain.

DR BENJAMIN CASTLEMAN She had occasional regurgitation but no nausea or vomiting.

DR SCHALL The pain was of long duration, at least several hours, and on one occasion it lasted all night. The patient noticed that lying down aggravated the pain. That is an important observation, but I should like to know whether swallowing while lying down caused pain.

From the history we have a story of pain followed by difficulty in swallowing. It would be well to consider what causes substernal pain and difficulty in swallowing. It has been estimated that at least 3 or 4 per cent of patients seeing a cardiologist because of substernal pain have pain due to disease of the gastrointestinal tract. In one series, a fifth of these gastrointestinal cases were due to disease of the esophagus. Could this be esophagospasm or cardiospasm? In these conditions, in contradistinction to angina, the pain is not related to effort. Atropine is beneficial. The pain in esophagospasm is of long duration, and x-ray examination demonstrates a dilated esophagus. When this dilated esophagus fills the patient may complain of a heavy substernal sensation and there may be regurgitation of food, which may be interpreted as vomiting, there may also be cough due to spilling over into the larynx. Pain and difficulty in swallowing may be due to congestion of the esophagus. In this condition the pain occurs in the recumbent position, and along with it there is difficulty in swallowing. Pain and difficulty in swallowing can be due to carcinoma of the esophagus, but in this condition the difficulty in swallowing usually comes first, there is a gradual closing of the esophagus due to the new growth, and the pain develops late. In this patient's history pain came first and then difficulty in swallowing. There was no cachexia, so that she probably had not had difficulty in swallowing over a long period of time. Esophageal hiatus hernia, that is, a hernia through the esophageal opening of the diaphragm, is usually painless, but it may start with pain, particularly if it is associated with an ulcer of the lower end of the esophagus or of the stomach. Difficulty in swallowing in esophageal hiatus hernia is not frequent but it may be present. In peptic ulcer of the esophagus the pain develops early and the difficulty in swallowing

comes later. The pain is substernal, and it may be referred to the epigastrium. It may also be referred to the dorsal spine, and occasionally it is widespread. Rarely the pain is referred to the ear, the face and the neck. Cases have also been described of esophageal ulcer with pain referred to the shoulder, arm and hand, but in contradistinction to anginal pain, the pain is present over the radial surface of the hand. The pain in esophageal ulcer is precipitated by swallowing and is worse in the recumbent position, because these ulcers are usually low in the esophagus and regurgitation of gastric secretion pre-

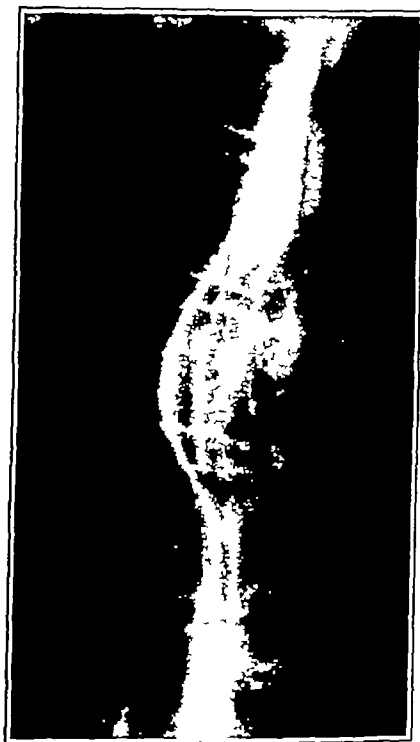


FIGURE 1

cipitates the pain. Diverticulum of the esophagus is usually without pain, but there is a sensation of pressure. It fills up, and then it may cause difficulty in swallowing merely by the filled pouch pressing on the esophagus. A traction diverticulum is usually discovered on routine x-ray examination. The patient rarely has symptoms, and there is often a history of mediastinal tuberculosis or tuberculosis of the spine.

Then we come to the x-ray interpretation. From the history as it is given, although it is stated that x-ray examination showed no apparent ulcer, I am inclined to think that this was an esophageal ulcer.

DR MILFORD D SCHULZ Ulcers of the esophagus are not always found.

DR SCHALL I know it. I am basing my diagnosis on the symptoms.

DR SCHULZ Here is the critical area, and the films taken in this hospital show the lesion described

ANATOMICAL DIAGNOSES

Small intestinal obstruction (jejunal), due to congenital diaphragm
Meconium peritonitis

PATHOLOGICAL DISCUSSION

DR CASTLEMAN It is unfortunate that this child was not brought into the hospital sooner and operated on, because at autopsy we found a lesion that surgically could have been removed, with probable cure of the patient. About 30 cm below the ligament of Treitz was a marked narrowing. The jejunum and duodenum above the obstruction were 5 cm in diameter, then the jejunum narrowed down to about 1 cm in diameter. At that point there was a diaphragm, in the center of which was an opening about 1 mm in diameter, the bowel beyond it was collapsed. This obviously was a congenital abnormality, which, during fetal life, had produced obstruction and a rupture somewhere above it. We were unable to find the point of perforation at autopsy, and this is almost the rule in these cases. We found numerous areas of calcification, practically all limited to the surface of the right lobe of the liver. We could not find any on the surface of the intestines, either grossly or microscopically, so that the perforation probably occurred in the duodenum close to the right lobe of the liver.

Microscopically the diaphragm was made up of connective tissue, with mucosa on each side and no muscle layer. The capsule of the liver was markedly thickened, and in it were the areas of calcification that were seen on the x-ray films. Surrounding some of them were cornified epithelial cells, and in one section there was a suggestion of true bone formation.

DR SIDNEY FARBER I should like to express my agreement with Dr Butler's conclusions and also with Dr Castleman's opinion that this process may go on to bone formation. When the site of perforation can be demonstrated, it is usually found about 10 cm proximal to the point of obstruction.

Dr Butler mentioned meconium ileus. There are two kinds. One type is caused by inspissated meconium produced by partial obstruction such

as that caused by stenosis at the ileocecal valve. Dehydration accounts for the inspissation. The pancreatic enzymes are normal. The second type or true meconium ileus is caused by failure of the pancreatic enzymes to enter the duodenum. The most frequent cause is atresia or stenosis of the pancreatic ducts. The abnormal meconium in such patients is so thick and mucilaginous that normal passage through the intestinal tract is impossible. Fatal intestinal obstruction within two or three days after birth is an invariable result of such obstruction. The abnormal meconium in patients with pancreatic achylia and true meconium ileus may be put into a watery condition in a test tube quite readily when mixed with a 1 per cent solution of pancreatin. In several cases Dr Robert Gross has been able to relieve the intestinal obstruction in babies with true meconium ileus by instilling into the small intestine such a solution of pancreatin. Complete relief of the intestinal obstruction took place, although intercurrent infection caused death days to weeks after the obstruction had been relieved. This method of therapy should be productive of successful results.

DR BUTLER Ladd and Gross⁴ give an excellent summary of the embryonic origin of diaphragms, persistence of which leads to partial rather than complete obstruction. In their book is a picture of a diaphragm that is identical with the one noted here.

DR CASTLEMAN Dr Schulz, is not this x-ray appearance pathognomonic of meconium peritonitis?

DR SCHULZ I do not know anything else that causes areas of calcification over the surface of the peritoneum.

DR CASTLEMAN Neuhauser,⁵ at the Children's Hospital, has reported 3 cases with exactly this appearance.

REFERENCES

- 1 Farber S. Congenital atresia of alimentary tract: diagnosis by microscopic examination of meconium. *J A M A* 106:1753, 1933.
- 2 Ladd W E, and Gross R E. *Abdominal Surgery of Infancy and Childhood*. 455 pp. Philadelphia: W B Saunders Company, 1941.
- 3 Farber S. Relation of pancreatic achylia to meconium ileus. *J Pediatr* 24:387-392, 1944.
- 4 Ladd and Gross.² P. 26.
- 5 Neuhauser E B D. Roentgen diagnosis of fetal meconium peritonitis. *Am J Roentgenol* 51:421-425, 1944.

Vomiting of a newborn infant in the first twenty-four hours of life is extremely rare. When it does occur, it suggests that the baby is seriously sick and deserves careful examination to find the cause. Certainly a flat plate of the abdomen should have been taken. One should also resort to the test introduced by Dr. Sidney Farber,¹—I blush to discuss this case with Dr. Farber in the audience,—which consists of examining the meconium to see if it contains cornified epithelial cells that the baby had ingested with the amniotic fluid. The presence of such cells in the meconium indicates that the intestinal tract is patent. If there are no such cells, the evidence is quite good that there is obstruction.

The baby's "stools became blue gray." Ladd and Gross² describe the stools in intestinal atresia as gray green. Throughout this history there is no indication whether the stools, which are mentioned at least twice, were small starvation stools, or whether they were large and contained milk curd. That information would be helpful to have.

Barium was given by mouth in the maternity hospital in an attempt to decide whether or not intestinal obstruction was present. In a newborn infant one does not have to resort to giving barium by mouth, and usually it is undesirable to do so. Certainly barium by mouth should not be given before a flat film of the abdomen is taken, and every effort should be made to make the diagnosis without giving barium.

Physical examination revealed a dehydrated youngster. Peristalsis was practically absent. As the child vomited fecal material, the intestinal obstruction would appear to have been fairly low.

DR. BENJAMIN CASTLEMAN: The record states that the baby vomited questionable fecal and bile-stained material. The stools were small and fecal.

DR. BUTLER: Then we are not so sure.

The next thing of note is the x-ray examination. I am sure that the films were taken immediately on admission to the hospital. There are two things of particular interest to look for in such patients: whether there is air in the peritoneal cavity and whether there are small areas of calcification. I wonder if we could see the x-ray films.

DR. MILFORD D. SCHULZ: You can see the barium in the stomach remaining from the examination done prior to admission to this hospital. The stomach is outlined by air, but if that air were free in the peritoneal cavity I believe that it would extend up over the liver, in other words, what is seen is probably air in the tremendously dilated loops of bowel. In the right lower quadrant is a large collection of barium that is obviously in a large dilated viscus. Here are tiny collections of opaque material plastered over the edge of the liver, along the peritoneal surface. They do not look like barium.

DR. BUTLER: I was going to ask whether the areas

of calcification appeared to be barium or the calcification that is seen in meconium peritonitis.

DR. SCHULZ: I should suspect the latter, if barium can get out of the bowel, air ought to be able to get out, and then if barium goes to the liver, air should also go there.

DR. BUTLER: So the x-ray films certainly confirm what is obvious from the story: namely, this patient had intestinal obstruction. Whether it was partial or complete remains to be seen. Furthermore, the x-ray studies suggest that this child had meconium peritonitis. It is too bad we do not have more information about the stools, both regarding the presence of cornified epithelial cells and the appearance of milk curds.

One might ask whether the intestinal obstruction was due to a congenital anomaly with atresia, to a congenital anomaly with stenosis or to meconium ileus. Dr. Farber³ has clearly described the obstruction due to meconium ileus and has correlated its occurrence with pancreatic achylia. Whatever the final picture, there was atresia of the bowel with obstruction. Whether it was congenital stenosis of the bowel with meconium or barium impacted above the obstruction or whether it was meconium ileus with pancreatic achylia does not at the moment affect the initial therapeutic procedure, which, of course, is operation. There are three things about the operation. First, the infant should have been operated on before the fifth day. Secondly, if atresia or stenosis is found, primary incision of that area and anastomosis, not enterostomy, is the procedure of choice, the reason being that in young infants atresia is frequently quite high in the gut and, if enterostomy is performed, one has a difficult time controlling nutrition and hydration. The third point concerns the use of pancreatic enzymes to dissolve the meconium, if at operation one finds meconium ileus on the basis of pancreatic achylia, in such cases there is an extremely tenacious meconium. I shall leave that aspect of the discussion to Dr. Farber.

My diagnosis in this case is intestinal obstruction, probably due either to stenosis or to atresia, aggravated by impaction of meconium and probably by some of the barium that was given and with meconium peritonitis and death before operation could be carried out.

CLINICAL DIAGNOSIS

Meconium peritonitis

DR. BUTLER'S DIAGNOSES

Intestinal obstruction due to congenital stenosis or atresia

Meconium peritonitis

directed toward the medical profession. An editorial in one of the newspapers stated that the physicians were less active, resourceful and persuasive than their opponents and that they did not make their strength felt fully, either as individuals or as a group. If this criticism is true, and there seems to be some justification for it, something surely should be done. Although there are certain explanations for this state of affairs, more true today than ever before because of the war, there can be no really legitimate excuse. The physician has sound knowledge in matters of this kind. Individually and as a group he must make himself heard and understood, particularly when the public welfare is at stake. This is a definite obligation.

The Chiropractic Bill remained in Governor Tobin's hands until July 20, when he returned it to the House with his veto attached. The following quotation from the Governor's veto message shows how clearly he understood the implications of this proposed law: "It would establish new and different standards of education and qualification for applicants seeking to practice in a field in which minimum standards are already established by statute. Thus it would introduce into the statutory system a double standard for the selection of practitioners in the field of medicine." It is to be hoped that when the Committee on Legislation submits its final report of the year, it will read into the record the Governor's veto message in its entirety.

For what was accomplished, due tribute should be paid to the Committee on Legislation of the Massachusetts Medical Society,—particularly to its tireless chairman, Dr. William E. Browne,—and to other members of the Society who gave generously of their time. The committee deserves well of the Society and what is still more important, it deserves well of the public at large.

CANINE

THE past prevalence of canine rabies, which flourished almost as a democratic institution in this Commonwealth until recent years, led to the adoption of certain standard practices. Chief among

these is the rule that any person bitten by an unidentified dog that escapes later detection must receive antirabic treatment. The more there are of unidentifiable dogs that roam our streets and byways, the oftener will it become necessary to invoke this rule of safety.

The incidence of dog rabies in Massachusetts, according to information furnished by the Commissioner of Public Health, has shown consistent improvement during the past dozen years, dropping from 331 cases in 1934 to 58 in 1938, to 20 in 1942, to 5 in 1943 and to 1 in 1944, with none, to date in 1945. The last case of human rabies occurred in 1935. The reason for this fall in incidence of dog rabies is not certain; it may have resulted from the preventive measures that have been adopted or it may simply reflect the natural rhythm in the rise and fall of the disease.

The history of rabies control in Massachusetts is of interest. Prior to 1934, it was attempted by area quarantine, but since the power of action is vested in the local communities and since there are over three hundred and fifty such political entities in the Commonwealth, concerted and co-operative action was never possible. In 1934 and subsequently, communities have been encouraged to organize dog-inoculation clinics, and perhaps because of the volume of such inoculations, it has been since 1934 that the decline in the disease rate has taken place. The present recommendation of the Department of Public Health is that communities in which cases of dog rabies have occurred, as well as contiguous communities, shall pass orders that no dogs be allowed on the streets, except on leash, unless they have been inoculated with antirabic vaccine within the previous year.

A considerable increase in the number of dogs untagged, uncollared and apparently unlicensed that are wandering in the streets of various municipalities of the Commonwealth has been noted. The stray dog is a potential health hazard, and in recognition of this fact the Commonwealth has for some time had a law requiring that all dogs be licensed and each community employ, under normal conditions, dog officers whose duty it is to apprehend, seize and dispose of unlicensed members of the canine family.

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THE 1945 LEGISLATURE

JULY 25 brought to a close another chapter in the legislative history of the Commonwealth. In many respects this session of the General Court was an unusual one — extraordinary because of its length and even more extraordinary, from the physician's point of view, because of the time and attention that it gave to subjects pertaining to medical practice.

Many controversial subjects were discussed by this legislative body, none, however, were more so than those that concerned the laws regarding the practice of medicine in the Commonwealth. Reason had a hard time with emotion. Many times, confusion of the Legislature seemed to be the object

aimed at. So innumerable were the red herrings drawn across the trail, that the trail itself was often obscured. The opposition set its stage skillfully, probably too much so, for as the lawyers put it, the case appeared to be "overtried."

It is gratifying that the major assaults on the Medical Practice Act were repulsed. These ranged all the way from further postponement of the effective date of the Approving Authority to its elimination. Furthermore, an attempt was made to set up a separate board of chiropractic, presided over by chiropractors, who would pass on the qualifications of those who would practice chiropractic in this state. Although this bill made no direct attack on the Medical Practice Act, it actually constituted a greater threat than all the other bills put together. In 1915, the Supreme Court of Massachusetts, in the case of *Commonwealth v. J. O. Zimmerman*, declared that the practice of chiropractic was the practice of medicine. The passage of this bill would have established a double standard for such practice and would have opened the way for innumerable healing cults to seek like concessions.

These bills were heard for the most part by either the Committee on Public Health or the Committee on Education, the former bearing most of the burden. The Honorable Joseph F. Montminy, senator from Lowell, presided over the Committee on Public Health with patience and good sense. The several bills having to do with the Approving Authority were finally consolidated by the committee itself into Bill 1980, which specifically exempted Middlesex University School of Medicine from the jurisdiction of the Approving Authority until July, 1949. This was reported favorably by the committee, Senator Montminy and Representatives Cutler, Vaughan and Harrington dissenting. This bill was voted on by the House on June 5, and by a vote of 148 to 74 was referred to the next General Court.

In the light of this action by the Legislature, it is difficult to understand why, on July 9, the House passed the Chiropractic Bill by a vote of 104 to 72. Subsequently the Senate concurred.

Curiously enough, it was not the House or the Senate that bore the brunt of the criticism that followed the passage of the Chiropractic Bill. Such criticism, and there was a good deal of it, was largely

The Chemistry and Pharmacy of Vegetable Drugs By Noel L. Allport, F.I.C., research chemist, British Drug Houses, Limited 8°, cloth, 252 pp., illustrated Brooklyn Chemical Publishing Company, Incorporated, 1944 \$4.75

This elementary treatise on the vegetable drugs should be of service to students of pharmacy and pharmacists. The pictures of the raw plant material are particularly interesting. An extensive index is appended to the text.

Atlas of the Blood in Children By Kenneth D. Blackfan, M.D., and Louis K. Diamond, M.D., assistant professor of pediatrics, Harvard Medical School, and visiting physician and hematologist, Infants' and Children's Hospitals, Boston. With illustrations by C. Merrill Leister, M.D., associate pediatrician, St. Luke's Hospital, Bethlehem, and Allentown General Hospital, Allentown, Pennsylvania 4°, cloth, 320 pp., with 70 plates and 19 charts. New York: The Commonwealth Fund, 1944 \$12.00

This atlas contains seventy illustrations in color of blood cells seen in normal and in pathologic states in infancy and in childhood. It is based on the blood changes observed in more than five thousand infants and children at the Hematology Laboratory at the Infants' and Children's Hospitals, Boston, since 1927. This vast experience with diseases of the blood in children has been condensed in this unique atlas. Since practically all the diseases affecting the blood in adults also occur in children, the work should be useful to the general practitioner, as well as to the pediatrician. The color plates are excellent, the text is well printed, and a selected bibliography is appended to the text. The work is recommended for all medical libraries.

Pastoral Work and Personal Counseling By Russell L. Dicks 12°, cloth, 230 pp. New York: The Macmillan Company, 1944 \$2.00

Mr. Dicks is an authority on pastoral counseling and in this new work has covered the whole field in its many and varying aspects and especially in relation to other professions. There is much of medical interest throughout the text, especially in those chapters having to deal with pastoral calls on the sick, those contemplating marriage and war neurotics. The last chapter considers the relations of the clergyman and other professional workers, such as the physician, the nurse and the social worker.

The Avitaminoses: The chemical, clinical and pathological aspects of the vitamin deficiency diseases By Walter H. Eddy, Ph.D., and Gilbert Dalldorf, M.D., pathologist of the Grasslands and Northern Westchester hospitals, Westchester County, New York. Third edition 8°, cloth, 438 pp., with 38 tables, 46 figures and 47 plates. Baltimore: Williams and Wilkins Company, 1944 \$4.50

The first edition of this authoritative text was published in 1937, followed by a second edition of 1941, and the authors now find it necessary to publish a third edition. The text has been rearranged to sharpen the separation between the deficiency diseases and the chemical nature and functions of the vitamins. The book is divided into three parts: the vitamins, treating of their nature and their function, the avitaminoses, in which the deficiencies of the various vitamins are considered, and technical methods: vitamin assay and vitamin values. The chapters on the chemical nature of the vitamins and cellular oxidation have been rewritten and much new material has been added, including many illustrations.

The Story of a Hospital: The Neurological Institute of New York, 1909-1938 By Charles A. Elsberg, M.D., 12°, cloth 174 pp., with 34 illustrations. New York: Harper and Brothers, 1944 \$3.50

Dr. Elsberg has written interestingly of the founding of the Neurological Institute in New York and of all its developments to the year 1938. The author has been associated with the institution from its beginning when the idea of an institution entirely devoted to the study and treatment of diseases of the nervous system was new in this country. At first, the hospital was housed in a building with small and poorly arranged accommodations for patients and little space for laboratories, but nevertheless considerable clinical research was done in these inadequate quarters. The new hos-

pital building was first used in 1929, and in 1955 the Department of Child Neurology was founded. The tenth chapter enumerates the contributions of the Institute to progress in neurology. Appended to the text are lists of trustees from 1909 to 1938 and of physicians and surgeons for the same period. This small book constitutes an important contribution to the history of neurology in the United States.

The Abortion Problem: Proceedings of the conference held under the auspices of the National Committee on Maternal Health, Incorporated, at the New York Academy of Medicine, June 19 and 20, 1942 Howard C. Taylor, Jr., M.D., conference chairman 8°, cloth, 182 pp. Baltimore: Williams and Wilkins Company, 1944 \$2.50

Abortion is a major problem in medicine, public health and sociology. At the conference, held in 1942, many authorities discussed the subject in its various aspects. The text is divided into four parts: the magnitude of the abortion problem, including the frequency of abortion and its effects on the general health of the individual, spontaneous abortion and its prevention, social, moral and economic causes, and control of the abortion problem. The legal aspects are considered in the last part. This valuable reference source should be in all medical, public-health, sociologic and legal libraries.

Lead Poisoning By Abraham Cantarow, M.D., associate professor of medicine, Jefferson Medical College, assistant physician, Jefferson Hospital, and biochemist, Jefferson Hospital, Philadelphia, and Max Trumper, Ph.D., lieutenant commander H-A(S), U.S.N.R., Naval Medical Research Institute, Bethesda, Maryland, and consultant in industrial toxicology, Cynwyd, Pennsylvania 8°, cloth, 264 pp., with 5 illustrations and 21 tables. Baltimore: Williams and Wilkins Company, 1944 \$3.00

Lead poisoning is probably one of the most important of the toxic hazards encountered in modern industry. Prior to World War II, about 750,000 tons of lead were annually produced and consumed in the United States and in 1940 about 54 per cent of the industrial plants in fifteen states were handling lead or its compounds. The physiology, pathology and clinical manifestations of lead are considered at length. There are special chapters on lead in the blood, body fluids and excretions, procedures for the determination of lead and the normal intake of lead. There is also a short chapter on the occurrence of chronic lead poisoning in industry. An extensive, selective bibliography is appended to the text. This comprehensive reference text should be in all medical and public-health libraries, as well as on the shelves of industrial physicians.

The Etiology, Diagnosis and Treatment of Amebiasis By Charles F. Craig, M.D. 8°, cloth 332 pp., with 45 illustrations and 10 tables. Baltimore: Williams and Wilkins Company, 1944 \$4.50

Dr. Craig in this new book has tried to include all the important data accumulated during the period since the publication of his earlier work in 1934. The book is well printed on good paper, and a selected list of references follows the text.

The Eclipse of a Mind By Alonzo Graves, M.D. 8°, cloth, 722 pp. New York: The Medical Journal Press, 1942 \$5.00

Autobiographies of sick persons, especially those afflicted with mental disorders, are of interest and value in the study of disease. This book records the life history of an extremely intelligent individual who throughout life had been afflicted with manic-depressive psychosis, having gone through eight attacks, five of which required complete hospitalization. Interspersed with the author's text are the hospital records of admission and discharge and also comments of the various physicians having charge of the patient. A unique feature of the presentation is the placing side by side, of hospital records of the patient's behavior and his explanations and elaboration of the same on recovery. The biography was written by the patient at the suggestion of the attending physician during the fourth hospitalization, and on the basis of the material obtained the evident gaps were filled in by replies to a series of questions. The patient recovered after

Dog rabies may never again become prevalent in this country, but if there is any circumstance that will favor its spread and make human antirabic treatments necessary it will be that of allowing unidentified dogs on the streets, and if there is any circumstance that will form a basis for control it will be the registration of all respectable canines, together with the disposal of all others

MEDICOLEGAL ABSTRACT

Liability for Malpractice X-ray treatment of pilonidal cyst, liability of an x-ray assistant
Two recent New Jersey decisions arose out of the same situation. The patient brought separate suits against Dr S and Dr C for alleged malpractice.

The jury found against Dr S. The patient introduced testimony having to do with x-ray therapy by witnesses who were licensed physicians but who did not hold themselves out as specialists in that branch of the profession. The court held that "having qualified as medical doctors, they [the physicians] are competent to testify on all medical subjects upon which they claim sufficient ability to express an opinion," so that the defendant could not exclude such testimony but only attempt to disclose by cross-examination that the witnesses did not possess sufficient knowledge.

The court held that the failure of Dr S's treatment might be evidence of his negligence. The trial judge had refused to charge that "the mere fact that treatment given in any case does not result satisfactorily or beneficially to the patient is not evidence of negligence." In sustaining the trial judge the court said:

The fact of nonbeneficial result may or may not be evidence of negligence. If despite proper diagnosis and treatment no benefit resulted no negligence could be charged, but if the treatment failed because of failure to exercise reasonable diligence, knowledge or skill, the result may be evidential of negligence.

The court, however, quoted with approval an earlier New Jersey decision as follows:

The physician in attending his patients, engages that he will use due care to discover the nature of the disease which gives occasion for his services, and in applying the usual remedies, but beyond this measure of skill and diligence the law makes no exaction. If he is to be held for results, or as a guarantor of success, it can be only in virtue of his express agreement.

The basis of the jury's verdict against Dr S was apparently either that he had given x-ray treatments for a condition that he had correctly diagnosed as a pilonidal cyst or that he had erroneously diagnosed as a furunculosis and that an excessive dosage of x-ray had been given.

The trial judge decided in favor of Dr C without

letting the case against him go to the jury, and the court sustained the trial judge. Under the court's view of the case the question was whether, on the evidence introduced by the patient, the jury could reasonably conclude that Dr C and Dr S were associates and engaged in a joint enterprise, so that each would be liable, and on that view the case is an interesting one on the existence of such a relation.

The patient's testimony was that he made an appointment to meet Dr S at his office and had never seen or heard of Dr C until he met him at Dr S's office. Dr S examined him with Dr C present but merely looking on. Dr S diagnosed the case and prescribed the quantity and frequency of x-ray treatment and administered all the six treatments given except the third and fourth. In the third and fourth Dr C handled the application to and removal from the patient's back of the machine. Arrangements concerning the amount of fees were made by the patient with Dr S, and all bills for services were payable to Dr S, made out on his billheads and paid by the patient to him or his secretary. There was no testimony that Dr C received any part of the fees paid by the patient to Dr S, or any proof of any advertisement that Dr C and Dr S held themselves out as associates, or any proof that Dr C in any way undertook to direct the treatment to be given the patient. Dr C merely continued the same treatment that had been prescribed and given by Dr S. The court held from these facts that it could not reasonably be concluded that Dr S and Dr C were associates and engaged in a joint enterprise in the care of the patient.

The language of the decision is guarded and leaves room for the possibility that if the question had been properly raised the evidence might have been sufficient to show a relation between Dr C and the patient by reason of which Dr C would have been liable for any negligence of his own — (*Young v Stevens*, 132 New Jersey Law 124, 39 Ail 2d 115 [1944], *Young v Crescente*, 132 New Jersey Law 223, 39 Ail 2nd 449 [1944]).

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

The Scholar and the Future of the Research Library: A problem and its solution. By Fremont Rider, librarian, Wesleyan University Library. 8°, cloth, 236 pp. New York: Hadham Press, 1944. \$4.00.

This special work stresses the use of microfilm in library work.

Studies from The Rockefeller Institute for Medical Research Reprints. Volume 126. 8°, paper, 574 pp., illustrated. New York: The Rockefeller Institute for Medical Research, 1944. \$2.00.

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THE RELATION BETWEEN VAGAL ACTIVITY AND AURICULAR FIBRILLATION IN VARIOUS CLINICAL CONDITIONS*

MARK D. ALTSCHULE, M.D.†

BOSTON

AURICULAR fibrillation is frequent in various forms of heart disease and in thyrotoxicosis, and its occurrence in other conditions is also recognized.¹ Although this arrhythmia is often encountered in clinical practice, its origin is not understood by most clinicians, in spite of the fact that it has been the subject of considerable fruitful study.

The available reports of studies in animals in which auricular fibrillation was regularly produced definitely establish the fact that vagal activity is one of the factors responsible for its occurrence.² The earlier studies on animals were not entirely satisfactory from a clinical point of view, since in all cases the experiments were performed under anesthesia, with the chest open and usually with electrodes and recording devices attached directly to the heart. It was therefore believed that similar experiments on normal, intact, unanesthetized animals might approach clinical conditions in man. Accordingly, the effect of the injection of acetyl- β -methyl choline, a substance closely related to the vagus hormone, was studied in one hundred experiments on 10 intact, unanesthetized dogs.² The drug was given intravenously in doses of 0.5 to 2.0 mg. In 3 dogs the only arrhythmia produced was partial heart block, whereas in the other 7 either auricular fibrillation or partial heart block occurred. In the latter group of animals it was impossible to predict which of the two arrhythmias would occur, since consecutive injections of the same dose of the drug might produce either. The heart block that occurred was characterized by the regular or irregular dropping of ventricular beats, whereas the P-R interval showed little change. No fatalities occurred during any of these studies, and one of the animals remained alive and well several years after having been subjected to these experiments. The animals that developed marked bradycardia resulting from heart block also exhibited Adams-Stokes

phenomena, recovery in every case occurred spontaneously. As a result of these studies it was considered to have been demonstrated that auricular fibrillation can be produced in intact animals by vagal hyperactivity. The alternative occurrence of auricular fibrillation or partial heart block was considered of great significance, and is discussed below.

Nahum and Hoff³ have shown that the intramuscular injection of acetyl- β -methyl choline in patients with thyrotoxicosis and a regular rhythm results in the development of transitory auricular fibrillation. Battro and Lanari^{4, 5} also produced auricular fibrillation in normal human subjects by means of the intracarotid injection of acetyl choline. In the present study, however, the use of these substances to attempt to induce auricular fibrillation in patients with heart disease and regular rhythm was considered too drastic a procedure and was not attempted. Accordingly, other studies on the relation between vagal activity and auricular fibrillation in man were undertaken.

It has been shown by Bruenn⁶ and by Keith⁷ that prolongation of the P-R interval in rheumatic heart disease is almost always due to vagal activity. A study was therefore made of the occurrence of auricular fibrillation in patients with this vagal arrhythmia.⁸ A high degree of correlation between the occurrence of partial heart block and auricular fibrillation in rheumatic heart disease was found. In 55 consecutive cases of a prolonged P-R interval, — transitory in 10 children and persistent for one month to eight years in the remainder, — 21 patients developed auricular fibrillation. Analysis of the sequence of electrocardiographic changes in the cases studied most thoroughly, such as the one covered by Table 1, showed that, initially, auricular fibrillation and low-grade heart block occurred alternately, with occasional periods of a normal P-R interval as well. If allowance is made for the fact that acetyl- β -methyl choline induces heart block, characterized in dogs by regularly or irregularly dropped beats, and in man by prolongation of the

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the fifth hospitalization and did not return for further treatment. The work is divided into three parts. The first deals with heredity and environment, marriage and consequences, and psychiatric interludes. Part two relates the story of seven attacks and four hospitalizations. The third part contains the author's reflections on his personality, including his sex life and his dream life, and his comments on mania and depression. The final chapter tells the story of the fifth hospitalization, the final attack before the patient's return to civil life. The story is written in a pleasing, narrative style and printed in good type on good paper. Such biographies are uncommon and should prove of exceptional value to psychiatrists and allied scientists and to human biologists. The book is recommended for medical libraries.

Interns Handbook A guide, especially in emergencies, for the intern and the physician in general practice. Prepared by members of the faculty of the College of Medicine, Syracuse University, under the direction of the Publication Committee, M S Dooley, M D, professor of pharmacology, and Maynard E. Holmes, M D, professor of clinical medicine, co-chairmen. Third edition. 16^o, cloth, 579 pp, with 15 tables and 15 figures. Philadelphia: J B Lippincott Company, 1944. \$3.00.

This handy manual, first published in 1929 and appearing in a second edition in 1938, has been thoroughly revised and should prove useful as a handbook of ready reference. The sections on chemotherapy, endocrine disturbances and the vitamins have been entirely rewritten. The subjects of pulmonary emboli and the vitamins are included for the first time. The text is divided into three parts: medicine, surgery and therapy. The therapeutic part includes a long list of well known drugs, with their therapeutic indications.

Beloved Crusader, Lawrence F Flick, Physician. By Ella M E Flick. 8^o, cloth, 390 pp, illustrated. Philadelphia: Dorrance and Company, 1944. \$3.50.

Dr Flick was a pioneer in the campaign against tuberculosis in the United States. He was a strong individual and as a crusader in this field naturally made many enemies, as well as friends. He was instrumental in founding the White Haven Sanatorium and the Phipps Institute in Philadelphia. He was responsible for bringing the international conference on tuberculosis to the United States in 1908. He was also active in congresses in foreign countries. In 1907 he made a trip as a delegate to the fourteenth International Conference of Hygiene held in Berlin, and it was at that time that he succeeded in obtaining the international congress for Philadelphia, for which Mr Henry Phipps guaranteed five thousand dollars for expenses. In 1909 Dr Flick traveled to Europe to study tuberculosis, and his diary of this trip comprises a chapter in the book. Dr Flick was greatly interested in history, and in 1884 he took a large part in organizing the American Catholic Historical Society of Philadelphia. This biography by his daughter is a worth-while contribution to the history of tuberculosis in the United States and the live factual story of a great man.

Sickness Indemnification. A panel discussion by R A Hohaus and others. Transactions Series, Bulletin No 1. 55 pp, 8^o, paper. Pittsburgh: Industrial Hygiene Foundation, 1944. Price on request.

This is a discussion on what is commonly known as health insurance. Three participating experts and the chairman dealt with the economic and administrative problems of group-health programs to employees and their families. Andrew T Court discusses the economic basis of health, in which he compares occupational and nonoccupational disability, bringing out the fact that disability from occupational causes is low and is being reduced, whereas nonoccupational disability has shown no improvement. Various interesting charts show how the increase of income above budget needs does not seem to improve health, death-rate trends indicate improvement in health of moderate-income groups. Increase of income above budget needs increases medical care moderately but inflates medical expenses. Short waiting periods result in increased sick claims of long duration, and the nursing of minor indisposition does not reduce serious sickness. Dr Gafaer discusses sickness indemnification and gives in

detail the experience of sick-benefit organizations connected with two public utilities and two iron and steel companies. There is also given in detail the data concerning sick-benefit organizations of eleven member companies of the industrial hygiene foundations.

Putting the Disabled Veteran Back to Work, II. A further panel discussion by C D Selby, M D, and others. Special Series, Bulletin No 3. 33 pp, 8^o, paper. Pittsburgh: Industrial Hygiene Foundation, 1944. Price on request.

This short pamphlet considers in order the following subjects: readjusting the veteran, vocational rehabilitation and placement of the veteran, new experiences in putting the disabled veteran back to work, and job-placement qualifications and guidance to disabled veterans returning to work. This timely pamphlet, as well as the preceding one, should prove useful to all physicians and others having to do with personnel in industry.

Fischerisms, Being a Sheaf of Sundry and Divers Utterances Culled from the Lectures of Martin H Fischer, Professor of Physiology in the University of Cincinnati. By Ray Marr. Third and enlarged edition. 24^o, cloth, 83 pp, with a frontispiece. Springfield, Illinois: Charles C Thomas, 1944. \$1.80.

The aphorisms of Professor Martin H Fischer, professor of physiology at the University of Cincinnati, were first published in 1930, and a later edition appeared in 1937. The third edition has been enlarged, by Ray Marr, by the addition of many new sayings added during the past seven years. The terse pithy statements collected in this volume were uttered by Professor Fischer during his lectures on physiology. They were collected mostly from the margins of the notebooks of students. This small volume is a welcomed addition to the collections of aphorisms of Osler and others. The volume is not for general circulation, having been privately printed for the students of Professor Fischer.

Personal Mental Hygiene. By Dom T V Moore, O S B, M D, Ph D, professor of psychology and psychiatry, Catholic University of America. 8^o, cloth, 331 pp. New York: Grune and Stratton, 1944. \$4.00.

This book is intended primarily for the individual, and because of this objective, the workings of the mind and its adjustments to life have been illustrated by an analysis not only of clinical material but also of various historical and literary personalities. The author points out the possibilities of ordinary emotional adjustment and at the same time brings into psychiatry the higher things of human life. It is an attempt to familiarize the individual with the possibility of emotional adjustment to the difficulties of life and also by a number of examples to provide a knowledge of wholesome attitudes of mind, ideas and principles.

The Marihuana Problem in the City of New York. Sociological, medical, psychological and pharmacological studies. By the Mayor's Committee on Marihuana. 8^o, cloth, 220 pp, with 53 tables. Lancaster, Pennsylvania: The Jaques Cattell Press, 1944. \$2.50.

This comprehensive study of a public-health problem was made by a special committee of the New York Academy of Medicine. All aspects of the drug are covered. A short historical sketch of the growth and usage of the drug, including the pertinent facts concerning hashish, precedes the text.

NOTICES

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, AUGUST 30

FRIDAY, AUGUST 31

*9-00-10-00 a.m. Medical clinic. Isolation Amphitheater. Children's Hospital.

10-50 a.m. Systemic Mycotic Infections. Dr Bernard Appel (Post graduate clinic in dermatology and syphilology). Amphitheater. Mallory Building. Boston City Hospital.

(Notices continued on page xx)

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FIBRIN FOAM AS A HEMOSTATIC AGENT IN SUPRAPUBIC PROSTATECTOMY*

WILLIAM C. QUINBY, M.D.,† AND ERNEST K. LANDSTEINER, M.D.‡

BOSTON

OF THE many problems presented by the operation of prostatectomy none are of more importance than that of the adequate control of bleeding from the prostatic cavity after the gland has been enucleated. Whether the prostate is approached through the urethra, by way of the perineum or by the suprapubic route, this problem remains of equal importance and difficulty. The literature of prostatic surgery abounds with many methods and devices for hemostasis that need no elaboration. In general at the present such devices consist of one sort or another of catheters and elastic dilatable bags, which after distention with fluid can be drawn down into the prostatic cavity and thus lessen the bleeding by pressure. Although these appliances are of considerable value, none are perfect, and the discomfort to the patient attendant on them is always an undesirable factor. Furthermore, the use of devices for hemostasis that must subsequently be removed contradicts the general surgical maxim that all bleeding should be adequately controlled before the wound is closed.

With the production of so-called "fibrin foam" by the Plasma Fractionation Laboratory of the Harvard Medical School,§ the opportunity arose to use this substance in the cavity left by removal of the prostate, as a new method of promoting complete

hemostasis, based on a sound physiologic principle. It seemed wise at the beginning to confine our observations entirely to the operation of prostatectomy by the suprapubic route in a single-stage procedure. The foam was used in pieces of convenient size that had previously been soaked in a solution of thrombin. It was held in place on the bleeding surface by a pledget of gauze over which negative pressure was made by suction through a tube. Four to six minutes of such pressure was sufficient to produce clotting and adhesion of the foam. On the advent of a satisfactorily dry prostatic bed,—on the average in ten to twenty minutes,—the bladder was closed by suture, leaving a mushroom catheter of small size (No. 18 Fr.) in the upper angle of the wound, so adjusted that the intravesical head of the catheter lay so far as possible from the area of operation. No other hemostatic agent was used, although in one case two rather large "spurters" were controlled by a stitch before the foam was put in place. In all cases, control of the bleeding by the foam was entirely adequate, much better than when pressure by bag was used, and in no case was there secondary bleeding.

Twelve patients form the basis of the present report of our experience with this substance thus far. The average age was sixty-nine years, and the average weight of the removed prostate 39 gm. The shortest time after operation in which the urine became clear on visual inspection was one day (2 cases), and the longest, six days (3 cases), in the remaining 7 cases the urine cleared in two or three days. The suprapubic catheter was removed in three to seven days, and the average time in which the wound healed and became dry was fifteen and a half days, the shortest period being eleven days and the longest twenty-four days.

*From the Urological Clinic of the Peter Bent Brigham Hospital.

†The products of plasma fractionation employed in this work were derived from blood collected by the American Red Cross by the Department of Physical Chemistry, Harvard Medical School, Boston, under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University.

‡Clinical professor of genitourinary surgery, emeritus, Harvard Medical School, acting urological surgeon, Peter Bent Brigham Hospital.

§Instructor in genitourinary surgery, Harvard Medical School, junior associate in genitourinary surgery, Peter Bent Brigham Hospital.

¶Prof. E. A., Jr. Development of fibrin foam as hemostatic agent in conjunction with human thrombin. *J Clin Investigation* 23:105-110 1944.

PR interval,⁹ a striking parallelism is seen to exist between the sequence of events in such cases of rheumatic heart disease and in dogs receiving a

TABLE 1 *Prolonged PR Interval and Auricular Fibrillation in a Case of Rheumatic Heart Disease*

DATE	RHYTHM	PR INTERVAL sec
1932		
Dec 6	Normal	0 24
Dec 30	Normal	0 18
1933		
April 12	Normal	0 20
1934		
April 3	Normal	0 22
Oct 11	Normal	0 24
1935		
April 8	Normal	0 30
June 19	Normal	0 24
Oct 9	Normal	0 22
1936		
Jan 4	Normal	0 26
June 29	Normal	0 24
Oct 7	Normal	0 26
1937		
June 1	Auricular fibrillation	
June 8	Auricular fibrillation	
June 21	Normal	0 26
June 30	Normal	0 28
July 13	Auricular fibrillation	

series of injections of acetyl- β -methyl choline. Both these reactions appear to be due to vagal action.

A similar study in patients with paroxysmal auricular fibrillation following myocardial infarction was made.¹⁰ Here again, a high degree of correlation between the occurrence of a prolonged PR interval and of auricular fibrillation was found, 9 of 14 cases with paroxysmal auricular fibrillation having a prolonged P-R interval as well. As yet, evidence proving the vagal origin of the changes in the PR interval in this condition is fragmentary, but in several cases studied atropine has been shown to abolish them. In single cases, such as the one shown in Table 2, the sequence of events was similar to

TABLE 2 *Prolonged PR Interval and Auricular Fibrillation in a Case of Myocardial Infarction*

DATE	RHYTHM	PR INTERVAL sec
October		
1	Myocardial infarction, auricular fibrillation	
2	Normal	0 20
5	Normal	0 16
18	Normal	0 16
25	Normal	0 24
November:		
1	Normal auricular fibrillation	0 22
2	Normal	0 18
3	Normal	0 20
5	Normal	0 22
23	Normal	0 18

that in the rheumatic subjects and in the dogs receiving acetyl- β -methyl choline that is, auricular fibrillation and partial heart block occurred alternately. A more recent study by Derow and Wolff¹¹ has shown that this relation between vagal hyperactivity and auricular fibrillation is also present in elderly patients with chronic coronary arterial disease. These authors also showed that in addition to partial heart block, sinus bradycardia may occur

at one time or another in patients who develop auricular fibrillation.

Reference has already been made to the work of Nahum and Hoff,³ which established the importance of vagal activity in precipitating auricular fibrillation in patients with thyrotoxicosis. Additional evidence of this connection is offered by the occasional occurrence of paroxysms of a prolonged PR interval alternating with those of auricular fibrillation in patients with hyperthyroidism. Two such cases with no evidence of organic heart disease have been observed in this clinic (Table 3).

Mines,¹² in his original work on circus movement in the heart, defined the conditions necessary for the development of auricular fibrillation as a shortened

TABLE 3 *Prolonged PR Interval and Auricular Fibrillation in 2 Cases of Thyrotoxicosis Without Organic Heart Disease*

NAME	AGE	DATE	RHYTHM	PR INTERVAL sec	BASAL META- BOLIC RATE per cent
M. S.	20	1933			
		Aug 7	Normal	0 22	+37
		Oct 11	Auricular fibrillation		+55
		Dec 5	Normal	0 22	+70
M. B.	58	1933			
		Mar 1	Auricular fibrillation	0 24	+23
		June 1	Normal	0 24	+28
		June 8	Normal	0 16	+27
		1936			
		Dec 3	Normal	0 18	- 3

refractory period and prolonged conduction time of the auricular myocardium. Stimulation of the vagus nerve shortens the refractory period of auricular muscle¹³⁻¹⁶ and thereby favors the occurrence of fibrillation. It is not unlikely, as Nahum and Hoff³ have suggested, that local inflammatory or metabolic changes in the auricle reinforce the tendency toward the occurrence of this, arrhythmia, which is initiated by vagal hyperactivity.

The source of the vagal impulses that give rise to prolongation of the PR interval and to auricular fibrillation in heart disease and thyrotoxicosis is obscure. It has been shown that vagal impulses that affect the heart reflexly may arise from the root of the aorta,¹⁷ the auricles of great veins¹⁸ and the lungs,^{19, 20} all of which may be involved in rheumatic inflammatory processes. In addition, congestive failure, by raising the auricular or venous pressure and causing pulmonary congestion, may also be a factor. These considerations do not, however, elucidate the origin of the vagal impulses causing cardiac arrhythmias in all cases of heart disease and in many cases of thyrotoxicosis.

SUMMARY

Evidence is presented that auricular fibrillation in certain types of heart disease and in thyrotoxicosis is a consequence of vagal activity. The origin of the vagal impulses that act reflexly on the heart to cause this arrhythmia is obscure.

difficult to use pieces of such grafts as so-called "postage-stamp" grafts Webster² has recently shown that phlo film may be used as a backing for

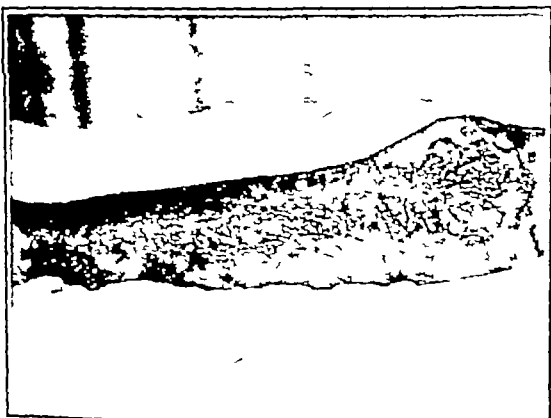


FIGURE 4 Recipient Site Ready for Grafting

grafts, and Evans³ has suggested cellophane for the same purpose

Before cutting a graft with a backing the drum is coated with dermatome cement and the backing film cemented to the drum as smoothly as possible. New coats of cement are then applied to the film and to the donor site and the graft cut as described by Padgett. The graft with its backing is removed from the drum and is placed on the recipient site. The backing prevents the normal contraction of the cut skin that results from its elasticity, and gives it added strength. The handling of the cut skin is consequently much easier, and any cutting of pieces to fit small or irregular areas is much more easily performed. Of more importance, how-

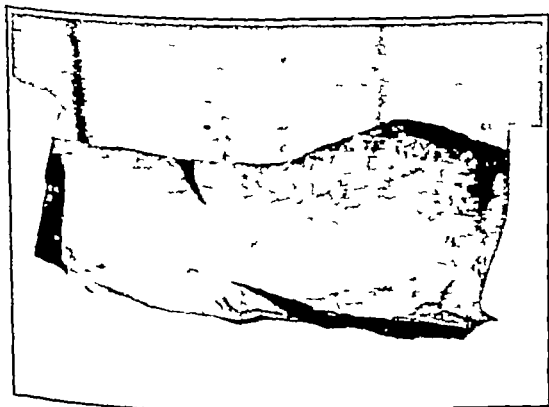


FIGURE 5 Graft in Place
Note the absence of sutures

ever, is the fact that no sutures are needed to maintain the graft at its original size and tension. The graft is maintained in place by even elastic pressure provided by a suitable pressure dressing, with or

without external splinting. The backing is easily peeled off after the graft has healed.

Experience with cellophane as a backing material has shown that it is very difficult to apply it to the dermatome without wrinkling. Even extremely small wrinkles cause irregularity in the thickness of the graft. A more serious difficulty is due to the relative stiffness of the cellophane and the graft. When attempts are made to fit the cellophane-backed graft to surfaces that are convex, concave, or irregular, wrinkling frequently results. This may result in the development of areas in which serum or blood collects beneath the graft because of poor approximation to the granulations, and over these areas the graft may be lost.

For some months, a fine-gauge nylon cloth* has been used for dressing the donor sites at skin-grafting operations in this hospital. A trial of this cloth in place of cellophane for skin-graft backing showed that it has qualities that made it desirable for this purpose. In the first place, it never wrinkles on the dermatome drum. Secondly, it sterilizes as

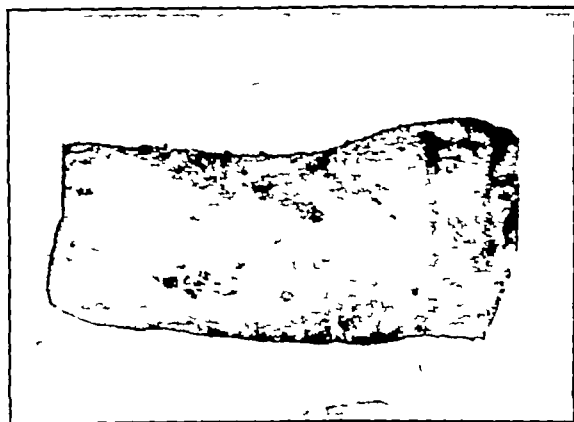


FIGURE 6 Graft at the Time of the Second Postoperative Dressing
Note the excellent "take"

easily as any textile and does not need special packing in the sterilizer to prevent adjacent surfaces from becoming adherent, as does cellophane. It is physically unchanged after sterilization. In spite of its relative limpness before being attached to the skin, it prevents contraction of the graft as well as does cellophane or sutures. Grafts backed with nylon conform better to irregular surfaces than do those backed with cellophane. In addition, it has been found possible to cut the skin 0.2 mm thick. Such grafts are slightly thinner than those that can be successfully cut and handled without backing. The donor sites from which such thin grafts have been taken heal quite rapidly and can

*This is the 1½-ounce nylon cloth used for parachutes. It is not over 0.1 mm thick and has a strength of 50 pounds per square inch in each direction. The warp is made of 40 Denier threads, one hundred and seven threads to the inch, and the weft of 60 Denier threads, seventy-eight to the inch. It was obtained from Textron Incorporated, Lowell, Massachusetts.

If spontaneous urination seemed a bit delayed, patency of the urethra was assured by the single passage of a sound of moderate size. Apparently the coagulated foam is not soluble in urine but after three or four days becomes disintegrated into a crumbling granular form, which passes easily through the urethra on urination. Postoperative irrigation of the bladder through the suprapubic catheter to remove small clots was carried out three times daily in the earlier cases, but with increased familiarity in the use of the foam it was possible in the last 3 cases to omit it.

There can be no doubt that by the use of foam as a

hemostatic agent in the operation of suprapubic prostatectomy the amount of blood lost is sharply diminished, the postoperative discomfort is lessened, the incidence of infection of the bladder is minimized, and the hospital stay is shortened.

SUMMARY

The use of fibrin foam as a hemostatic agent following suprapubic prostatectomy is described.

Because of the excellent results obtained in 12 cases, this means of controlling postoperative hemorrhage appears preferable to any method previously employed.

CLINICAL NOTES

NYLON BACKING FOR DERMATOME GRAFTS*

ROSS W. GREEN, M.D.,†
STANLEY M. LEVENSON, M.D.,‡
AND CHARLES C. LUND, M.D.§

BOSTON

EXPERIENCE with many skin-grafting operations in the repair of burn wounds of all sizes has shown that the Padgett dermatome technique gives extremely satisfactory results but is time-

the periphery of the graft. Frequently the suturing is the lengthiest part of the operation and thereby

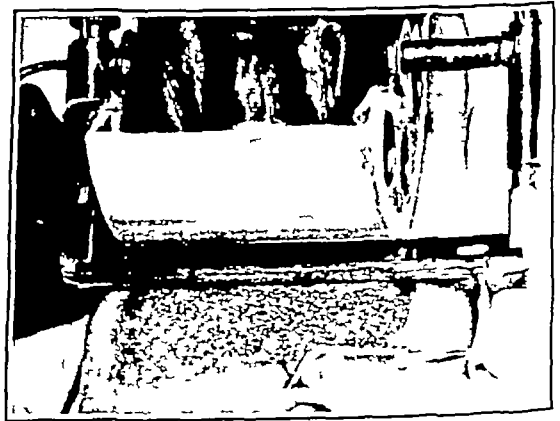


FIGURE 2 Graft Being Cut from the Donor Site

increases the seriousness of the procedure. In addition, considerable care must be taken in the

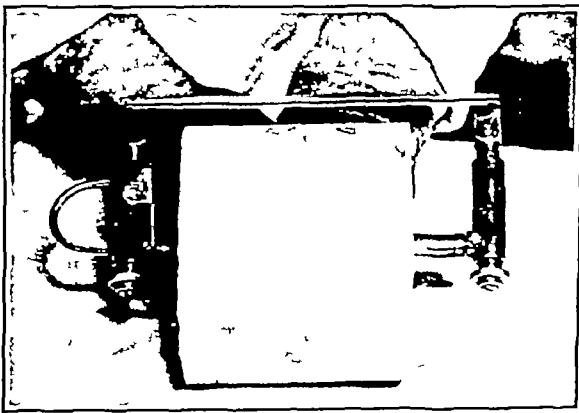


FIGURE 1 Nylon Cemented to the Drum

consuming. To secure properly stretched grafts in place it is necessary to place many sutures at

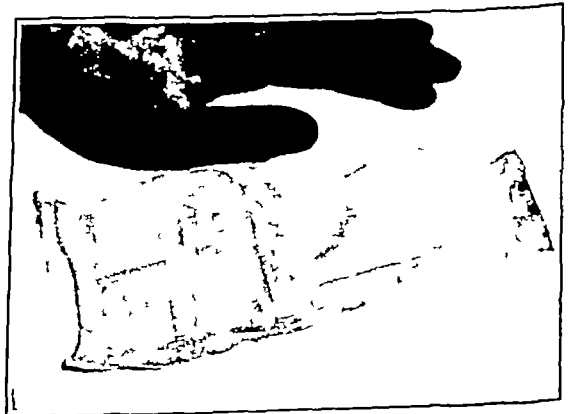


FIGURE 3 Cut Graft with Nylon Backing

Note the limpness of the graft, yet the normal tension of the skin is maintained.

removal of the graft from the drum to prevent curling and wrinkling. For the same reason, it is

*From the Burn Assignment of the Surgical Services, the Thorndike Memorial Laboratory, and the Second and Fourth Medical Services (Harvard) Boston City Hospital, and the Departments of Medicine and Surgery of the Harvard Medical School.

The work described in this paper was done, under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

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drug, he was taking 120 mg daily, by the end of the 3rd year 150 mg, by the end of the 4th year 180 mg, and by the end of the 5th year 250 mg. He obtained prescriptions for the drug by consulting several physicians who did not realize that he had become an addict. He continued the use of the drug until the day of admission.

During the 5 years of addiction to amphetamine sulfate, the patient was able to work daily as a guard in a war plant, did some law practice in the evenings, and ate and slept well. Four months before admission he began to show mental symptoms in the form of sleeplessness at night and restlessness at work. He soon began to complain that searchlights were being thrown into his bedroom and felt sure that his home was being watched. Two weeks later he complained to his wife that his car was being followed when he was traveling to and from work — at first by one automobile but soon by at least six cars. This feeling was so real that he drove his car by devious routes to elude his pursuers, but without success. Finally he became so fearful that he left his job. On two occasions he asked the police to investigate prowlers about his home. One month before admission, he began to hear the voice of his son, who was in the armed forces in Europe. He interpreted the stars in the sky as signal lights coming from his son, who he thought was flying in an invisible helicopter. He would spend hours in the evenings looking at the sky and conversing with his son, and expected that the latter would visit him at any moment. On one occasion he prepared a meal for the boy and his commanding officer and waited for them for hours. In an effort to explain his experiences, he developed the theory that he was being tested by the Government for an important secret-service position. Finally he became so hyperactive, sleepless and fearful that hospitalization was advised. He had lost 20 pounds in weight during the 5 months prior to admission.

The physical examination on admission was essentially negative. The weight was 172 pounds and the blood pressure 140/90. The heart and lungs were normal. Neurologic examination was negative and the blood picture was normal. A blood Hinton reaction was negative.

Mentally the patient was oriented in all spheres but had to insight into his condition and violently protested against what he felt was illegal commitment. He freely admitted having seen and heard his son outside his home and the admitting office. He remained excited, agitated, resistive, hallucinated and deluded, and refused food for 6 days. He required sedation for sleep. On the 7th day, he became more co-operative and took food, but stated that he could still see his son's airplane in the sky. He argued that since it would be possible for his son to be in a plane in this neighborhood, it would therefore be possible to see him, and that thus his experiences were not necessarily hallucinations. He frequently demanded that his wife engage an attorney and obtain his immediate release. He gradually became more and more co-operative and friendly, sought frequent interviews with the physicians, and in a short time readily accepted the fact that his unusual experiences were the result of his long-standing addiction. He still expressed the belief, however, that some of his experiences were real.

Three weeks after admission, he admitted that at night he looked at the sky with the hope that he would see some signal from his son's airplane. At that time he tended to be slightly euphoric, readily boasting about his past experiences with women and alcohol and admitting that he had been addicted to alcohol for years and had exchanged the liquor for amphetamine sulfate. He evidenced no real insight into his condition and insisted that hospitalization was no longer necessary to cure him of his addiction. He had no conception of the underlying personality deviations that early in life had led to his behavior pattern.

By the 4th week in the hospital, he had developed good insight into his past experiences, and had also begun to realize that he would be benefited by psychiatric guidance after leaving the hospital. He had gained 7 pounds in weight.

On the 30th day, the patient was discharged as recovered, the diagnosis being "psychosis due to drugs and other exogenous toxins (amphetamine sulfate)."

This case of acute hallucinosis in an amphetamine sulfate addict is of special interest because the patient was able to ingest extremely large doses of the drug over a long period of time without suffering any apparent physical ill effects. After almost five years of addiction, mental symptoms developed. There was no loss of weight until the mental symptoms appeared, and no rise in blood pressure was noted. This addiction occurred in a man who had previously been addicted to alcohol and who had shown many neurotic traits.

From an analytical viewpoint, the alcoholic addict and the drug addict present many psychogenic factors occurring early in life, arresting emotional development at the oral erotic stage. Childhood frustrations and loss of mother love, bringing with them feelings of insecurity and inferiority, are well recognized factors in the production of alcoholic addiction. The childhood of this patient was unhappy, with considerable emotional trauma from the time of his mother's death to adolescence. His excessive smoking, love of sweets, drinking, early sex experiences, choice of profession, talkativeness and, finally, drug addiction are all a part of an oral erotic pattern of behavior. The acute mental symptoms presented closely resembled those seen in acute alcoholic psychoses. The visual hallucinations were the most prominent ones. With the disappearance of these experiences, the patient showed no evidence of the depression that usually follows in alcoholic psychosis.

This case strongly confirms the conclusions of Reifenstein and Davidoff⁷ that psychoneurotic patients and alcoholic addicts are prone to become addicted to the use of amphetamine sulfate. The use of the drug in the treatment of alcoholic addiction should be limited to hospitalized cases.

SUMMARY

A case of acute hallucinosis in a patient who was addicted to amphetamine (Benzedrine) sulfate and formerly to alcohol is presented and discussed.

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be used again in a relatively short time. On all areas where split-thickness grafts are indicated, grafts of this thickness have given satisfactory end results.

The following case illustrates the use of this technic.

M P, an 11-year-old boy, was admitted on November 18, 1944, shortly after receiving flame burns of the entire lower right leg, the total third-degree area being 6 per cent. The surface treatment on entry consisted in the application of a dry, sterile pressure dressing without preliminary cleansing. These dressings were freshly applied every 2 weeks. On the 59th day, two dermatome drums of nylon cemented grafts were removed from the abdomen and left thigh and applied to the granulating areas. A firm pressure dressing with a plaster cast was applied. On the 7th postoperative day, the dressings were removed. The "take" of the graft was found to be excellent. Figures 1-6 illustrate the operative technic used.

SUMMARY

A technic employing nylon for the backing of dermatome grafts is described.

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ACUTE HALLUCINOSIS AS A COMPLICATION OF ADDICTION TO AMPHETAMINE SULFATE

REPORT OF A CASE

JACOB NORMAN, M.D.,* AND JOHN T. SHEA, M.D.†

FOXBOROUGH, MASSACHUSETTS

AMPHETAMINE (Benzedrine) sulfate has been widely used in recent years in the treatment of chronic alcoholism,¹ with or without psychosis of narcolepsy and of depression, because of its stimulating action on the central nervous system. Its therapeutic action is to enhance mental activity and increase ability to concentrate; it lessens the feeling of fatigue and elevates the mood.

The toxic effect of amphetamine sulfate varies a great deal in different persons.² Small doses may produce alarming symptoms, whereas it is reported that large doses taken over a period of years for narcolepsy have produced no apparent ill effects.

Apfelberg³ reported the case of a man who remained in coma for thirty-six hours after taking 140 mg. of amphetamine sulfate. Two fatal cases have been reported in the literature^{4, 5}—one was that of a 25-year-old student who collapsed and died after taking 30 mg. of the drug daily for a few days, and the other that of a child of one year who died after the accidental ingestion of 40 mg.

Goodman and Gilman⁶ state that the most frequent toxic effects are restlessness, insomnia, talka-

tiveness, irritability, confusion, hallucinations and delusions.

Reifenstein and Davidoff⁷ reported a series of cases of alcoholic psychosis treated successfully with amphetamine sulfate. Miller⁸ gave the drug to a large group of patients with chronic alcoholism without apparent ill effects or addiction. Reifenstein and Davidoff strongly advise that the drug be limited to institutionalized cases, because of its tendency to produce addiction and the relatively frequent and unpredictable occurrences of serious toxic reactions. They have observed that there is a tendency toward addiction to amphetamine sulfate in neurotic patients and in those addicted to alcohol, morphine and cocaine.

CASE REPORT

A B (F S H), a 49-year-old lawyer of Irish descent, was admitted to the Foxboro State Hospital on February 10, 1945, with somatic, visual and auditory hallucinations of 4 months' duration. He was hyperactive, suspicious and belligerent. He admitted having taken amphetamine sulfate in steadily increasing doses for the last 5 years, and had reached a maximum daily dosage of 250 mg.

The patient's mother died of tuberculosis when he was 2 years of age. The father was an alcoholic addict and died at 60. An older brother died of tuberculosis, and a sister met accidental death at 27. The patient was reared by a childless aunt, who demanded rigid discipline.

The patient's birth was normal, and he had the usual childhood diseases. His progress in school was average, and at the end of the 2nd year of high school, at the age of 16, he left of his own volition, taking a job as a grocery clerk. Five years later he resumed his studies, attending night school, and later received his high-school diploma. He then studied law for 4 years and passed the bar examinations. He was well liked, made friends readily, was successful in his practice, and became quite active in local and state politics. Circumcision was performed at 12 years of age and appendectomy in 1933.

At the age of 12, the patient had his first heterosexual experience, following which he developed a penile infection and was circumcised. Between the ages of 17 and 25 he had frequent sexual experiences with various married women, toward whom he formed no emotional attachments. He married at 25 years and made a fairly good sexual adjustment. He had 2 children, a son of 23 and a daughter of 13. He admitted occasional extramarital relations, about which he felt no guilt. During the period of addiction to amphetamine sulfate his sexual desires and potency were increased.

The patient had been a heavy smoker since an early age, consuming thirty to forty cigarettes a day. For years he had been excessively fond of sweets. He began to use alcoholic beverages at the age of 17. At first he drank only on week ends, but the habit soon became a daily one. When he took up the study of law, he ceased drinking, abstaining completely for 5 years, but as soon as he began practice he resumed his drinking habits and continued to drink steadily for 7 years. After 5 years of successful practice of law, he met with severe financial reverses, owing to the economic crisis prevailing at that time, to speculation and to loss of clients on account of his alcoholic habits. After struggling for 2 years he gave up his law office and political and social activities and accepted employment on a WPA project. During the latter part of his heavy drinking periods the patient was frequently intoxicated and was twice arrested for driving under the influence of liquor, but at no time did he develop any symptoms of alcoholic psychosis.

In 1939 the patient consulted a physician because of fatigue and vague gastrointestinal symptoms, which he described as "an all-gone feeling." Amphetamine sulfate was prescribed, 10 mg. four times daily. The effect of the drug was so stimulating that he gave up the use of alcohol and did not return to it. He continued to take amphetamine sulfate, but gradually increased the daily dosage without the consent of his physician. By the end of the 2nd year of use of this

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Rorschach method, and situational factors that might have produced or aggravated psychoneurotic symptoms. In patients with localized headache, these symptoms appeared to be more closely related to brain damage than to psychologic factors. Studies of postural vascular responses indicated no effects in patients with head injury different from those in psychoneurotic patients or in those convalescing from other illnesses. A follow-up study of 82 patients previously treated at the Montreal Neurological Institute showed that the long-term results with spinal or cranial subdural insufflation have been no better than those following pneumoencephalography, and that for none of these patients could the influence of other factors be ruled out. The authors emphasize the relation between psychologic and physical factors in the production of the symptoms after head injury and the need of considering the person as a whole in the prevention and cure of post-traumatic symptoms.

The factors influencing the development of the post-traumatic syndrome are discussed in a series of papers from the Boston City Hospital where 200 patients were observed for a number of months following an acute head injury. Brenner, Friedman, Merritt and Denny-Brown¹¹ found that headache was present at some time after the injury in 69 per cent of the patients, and that it persisted for longer than two months after the injury in 32 per cent. These headaches were characteristically associated with dizziness and nervous symptoms — fears, anxiety, fatigue, irritability and inability to concentrate. The incidence of prolonged headaches was high among patients with nervous or neurotic symptoms prior to injury, those with complicating environmental factors, — including compensation, — those with symptoms of marked immediate emotional reaction to the injury and those with scalp lacerations. It was low among the victims of recreational accidents and in cases in which the head injury was mild. Neither changes in the spinal fluid, the electroencephalogram or the reflexes nor the extent of disorder of consciousness immediately after the injury gave adequate prognosis of subsequent liability to headache. Headache was, however, significantly less frequent in those who had no initial disorder of consciousness.

Friedman and Brenner,¹² in a study of 22 patients with post-traumatic headache, were able to produce headaches identical in character and location by the intravenous injection of histamine. They conclude that it is possible that histamine activates the physiologic mechanism involved in the production of some types of post-traumatic headache.

The symptoms of post-traumatic vertigo and dizziness were subjected to an analysis by Friedman, Brenner and Denny-Brown,¹³ who found them in 51 per cent of 200 patients at some time after the injury and in 34 per cent after discharge from the hospital. True vertigo was present in only 6 per

cent. There was little evidence that post-traumatic dizziness was related to damage to the vestibular end organ. This study showed that both physical and psychologic factors played an important role in the production of prolonged post-traumatic dizziness, since this symptom was characteristically associated with various factors of psychiatric significance such as pretraumatic nervousness and complicating environmental factors during convalescence. It was more frequent in patients with a severe head injury as evidenced by prolonged coma or post-traumatic amnesia.

The factors of importance with regard to disability following head injury in this series were analyzed by Denny-Brown.¹⁴ One hundred and ten (55 per cent) of the patients complained of symptoms after discharge from the hospital. The symptoms were related to a structural physical disorder in 16 patients, to psychiatric symptoms in 70, to headache in 81 and to dizziness in 68. These symptoms were frequently associated, but each occurred alone. The association of headache, dizziness and psychiatric symptoms — the so-called "postconcussion syndrome" — occurred in 30 patients. Factors of unfavorable prognostic significance in relation to return to work within two months and within six months of the injury were analyzed, and in each case features indicative of severity of injury and those indicative of psychologic stress were intermingled. The symptoms associated with prolonged disability, whether the injury had been severe or mild, were predominantly mental symptoms related to anxiety. Denny-Brown concludes that the environmental factors of injury were in total effect more important in accounting for disability than were the factors indicative of severity of injury, but that neither can be neglected in the assessment of prognosis. He adds that the extensive association between head injury and psychiatric factors indicates possibilities for lessening disability by psychiatric treatment.

Adler¹⁵ found mental symptoms in 31.5 per cent of 200 patients with head injuries. Mental symptoms particularly anxiety, were, with headache and dizziness, the most frequent symptoms in convalescence and were the major cause of disability, particularly prolonged disability, following head injury. A number of factors entered into the production of the anxiety symptoms in these patients, the most direct being reproduction of fears related to the injury and elaboration of pre-existing conflicts in relation to social and occupational adjustment.

The relative infrequency of head injury as a cause of serious mental deterioration or a real psychosis is emphasized by the studies of Denny-Brown,¹⁴ Adler¹⁵ and Thompson and McGinnis.¹⁶ The last authors found that only 174 (0.28 per cent) of 61,795 patients admitted to a psychopathic hospital were diagnosed as suffering from post-traumatic

MEDICAL PROGRESS

NEUROLOGY

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SOME of the recent significant advances and refinements that concern neurology are discussed in the following sections

ELECTROENCEPHALOGRAPHY

The value of the electroencephalogram in convulsive disorders, head injuries and brain tumors has been well established for some time. In recent years the attention of investigators has turned to a great variety of other conditions, and the literature of the past year contains a large number of reports on the results of the use of the electroencephalogram in cases of alcoholism, delirium, behavior problems in children, psychopathic personality, psychoneurosis, psychosis, migraine and cerebral arteriosclerosis, as well as further studies in cases of epilepsy and brain tumor.

Cobb¹ reports correct localization in 58 per cent of 120 cases of intracranial tumors and abscesses. The tumors that lend themselves most readily to localization are those on the free convexity that are rapidly growing, but even among these there are some that show only a diffuse abnormality. The records in cases with increased intracranial pressure were variable and were more closely related to the degree of consciousness than to the height of the intracranial pressure. The ideal method of localization was the finding of phase-reversal of slow waves, but not infrequently it was necessary to depend on their maximum intensity. It was suggested that the 4-to-7 per second frequency band, or theta rhythm, is associated with lesions in the region of the third ventricle.

Walter and Dovey² in a study of subcortical tumors found that in deep tumors spreading outward the main feature was 6-cycle per second activity from the cortex above the tumor or from the parietotemporal regions or both. A small delta rhythm was sometimes seen immediately above the tumor. In cases with deep tumors not affecting the cortex, the 6-cycle activity was the only significant abnormality. These so-called "theta rhythms" were characteristic of the resting, immature or isolated parietotemporal cortex.

Williams,³ in a study at the Military Hospital for Head Injuries in England, found that larval epileptic outbursts in the electroencephalogram were invariably associated with overt fits, but also that less well defined outbursts were frequently associated with them. These disturbances were found in 25

per cent of 210 cases of post-traumatic epilepsy, as compared with 56 per cent of 275 cases of apparently idiopathic epilepsy. The presence of the typical larval epileptic patterns and other paroxysmal outbursts in the electroencephalogram of patients with head injury usually indicated that clinical seizures would develop later.

Changes in the electroencephalogram in alcoholism are reported by Greenblatt, Levin and di Cori⁴ and by Engel and Rosenbaum.⁵ Greenblatt and his associates found that chronic alcoholism with psychosis was associated with a higher than normal incidence of electroencephalographic abnormalities. Confusion or hallucination was frequently associated with electroencephalographic abnormalities, which tended toward normal with the disappearance of the confusion or hallucination. Engel and Rosenbaum induced acute intoxication in 7 normal subjects with normal electroencephalograms, and noted that this state was accompanied by progressive slowing of the brain waves. The degree of slowing was more significant than the development of any particular wave frequency.

Abnormalities in the electroencephalogram in 49 per cent of 67 children with primary behavior disorders were reported by Gottlieb, Knott and Ashby,⁶ and in 54 per cent of 68 psychopathic personalities by Knott and Gottlieb.⁷ Pacella, Polatin and Nagler⁸ found abnormalities in the electroencephalogram in 64 per cent of 31 patients with obsessive compulsive states.

Irregular slow waves were recorded by Engel, Ferris and Romano,⁹ from the contralateral occipital cortex of 3 patients with scintillating scotoma and homonymous visual-field defect during attacks of migraine. Normal activity was recorded from the ipsilateral occipital cortex and other portions of the brain at the same time.

POST-TRAUMATIC SYNDROME

The frequency of head injuries in the war has led to a number of studies on the post-traumatic syndrome. Ross and McNaughton¹⁰ studied 90 patients, both civilian and military, several months following an injury to the head. A comparison of the 68 patients who had persistent symptoms was made with the 22 who had no complaints. Attention was given to the type of headache, the pre-traumatic personality, the severity of the injury, reports of electroencephalographic and pneumoencephalographic abnormalities, certain ratings of instability and disability as determined by the

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there was some improvement except in 2 per cent of the private patients and 4 per cent of the industrial-compensation cases

Botterell, Keith and Stewart,²⁵ in reporting the management of sciatica due to herniation of the intervertebral disk in Canadian soldiers overseas, stated that they began with a three-week period of conservative treatment, with complete rest in bed. If there was not sufficient improvement to allow patients to re-engage in their regular duties or in those of a less strenuous character, operation was performed, this being done in 51 men. Following operation 29 returned to full duty and 14 to sedentary duty, and 8 were found to be unfit for military duty of any kind.

There was complete relief of pain in 65 per cent of the 400 patients operated on by Poppen.²⁰ There was no improvement in 15 per cent. Sixty per cent of the patients were able to return to their usual activities within six months of the operation, and an additional 35 per cent returned in the next six months. Poppen stresses the fact that the greatest improvement concerned the sciatic pain, relief of which was obtained in 90 per cent of the cases. Low-back discomfort persisted in a large percentage — in 40 per cent when tired and in 60 per cent when attempting to do heavy lifting.

Cervical Disks

Herniation of intervertebral disks in the cervical region is much less frequent than that in the lumbar, and the syndromes produced are less well understood. Michelsen and Mixter²⁶ state that cord compression as a diagnostic criterion of cervical herniation has been overemphasized and that involvement of nerve roots is more frequent. They report 8 cases with a clinical syndrome characterized by root pain and local segmental sensory disturbance, localized muscle atrophy and weakness, absence of cervical lordosis and narrowing of the sixth cervical interspace as seen by x-ray and filling defects following the injection of lipiodol. All the patients had received various types of therapy without benefit. Six were completely relieved of their symptoms by removal of the disk fragments at laminectomy. In 1 case in which this was impossible, the patient was relieved of pain but motor disability persisted. In the remaining patient there was no relief of symptoms following operation.

Twelve cases of rupture of the disk in the cervical region are reported from the Walter Reed Hospital by Spurling and Scoville.²⁷ These authors found that percussion of the spine in the region of the affected disk or tilting of the head and neck to the affected side reproduced the characteristic pain. Complete relief of symptoms resulted from operative removal of the disk fragments in all these cases.

Similar reports on the cervical-disk syndrome are made by Ulmer and Meredith,²⁸ Bucy and

Chenault,²⁹ Elliott and Kremer³⁰ and Browder and Watson.³¹

USE OF PENICILLIN IN INFECTIONS OF THE NERVOUS SYSTEM

During the past year there have been a number of reports on the results of the use of penicillin in infections of the nervous system. Most forms of bacterial meningitis respond to this drug, but the results obtained in meningococcal meningitis have been no better than those achieved with the sulfonamide drugs, and perhaps not so good. Several cases of cavernous sinus thrombosis have been cured. There are also a few preliminary reports on penicillin in the treatment of syphilis of the nervous system.

The amount of the drug that should be used in these various infections and the best route of administration have not as yet been determined. Many authors think that intraspinal administration is necessary because only small amounts of penicillin are present in the cerebrospinal fluid after intramuscular or intravenous injection. The intraspinal injection of penicillin may be followed by symptoms and signs of injury to the roots of the cauda equina and the spinal cord.³² Two deaths as the result of encephalopathy following intracisternal injection of the drug were reported by Neymann, Heilbrunn and Youmans.³³ Application of penicillin to the brain cortex of man or animals may produce convulsive seizures.³⁴ It is my own opinion that the therapeutic value of any drug for infections of the nervous system is not necessarily related to the amount found in the cerebrospinal fluid. It may be necessary to use heroic methods of treatment in potentially fatal diseases, such as pneumococcal meningitis, but in less serious conditions it seems wise at the present state of knowledge to avoid the use of penicillin intraspinaly or intracisternally if other forms of therapy are available.

Meningitis

Rosenberg and Arling³⁵ treated with penicillin 65 patients with meningococcal meningitis at the Great Lakes Naval Hospital, with recovery of 64. The drug was administered intrathecally and intravenously or intramuscularly. In the majority of the patients one or two intrathecal injections of 10,000 units were sufficient, but in several cases four or five injections were needed. No serious untoward effects were noted from the injection of 10,000 units intraspinaly, but the use of larger amounts produced symptoms and signs of meningeal irritation that were severe enough to contraindicate their use. In addition to the intraspinal treatment the patients were given the drug intravenously or intramuscularly, the total dosages by these routes ranging from 20,000 to 900,000 units. The ordinary complications of meningococcal infection — acute monoarthritis, polyarthritis, or

psychoses Abnormalities in neurologic examination were present in 66 per cent The mental impairment presumably due to the head injury was aggravated in some of the patients by complicating factors, such as arteriosclerosis, advancing age, alcoholism and a post-traumatic convulsive state

CAUSALGIA

Injuries to the extremities in the war have awakened an interest in this troublesome problem Recent studies have clearly shown that the symptoms present in patients with causalgia are related to an injury to sympathetic nerve fibers and that this can be relieved by sympathectomy

Speigel and Milowsky¹⁷ found causalgic symptoms in 9 of 275 patients with peripheral nerve injuries examined at the Schick General Hospital in Clinton, Ohio In 8 of these cases the injury was to nerves in the upper extremity, — the brachial plexus in 2, the ulnar in 2, the median in 1, the radial in 2 and the ulnar and median in 1, in 1 case the saphenous nerve was affected Injury to blood vessels was frequently present but was not necessary for the production of the syndrome Complete relief of symptoms was obtained in 7 cases by surgical sympathectomy One patient was relieved by procaine block and 1 by alcohol block of the involved sympathetic nerves The authors emphasize the importance of the early use of diagnostic sympathetic block, followed by surgical sympathectomy Neurolysis, nerve section and periarterial sympathectomy were of no therapeutic value

Mayfield and Devine¹⁸ report 15 cases of causalgia in 737 patients with peripheral nerve injuries who were treated at the Percy Jones General Hospital in Battle Creek, Michigan The nerves involved were the median in 7, the median and ulnar in 1, the brachial plexus in 1 and the sciatic in 6 The lesion of the nerves was incomplete in all cases Certain patients showed vasoconstriction in the causalgic limb, others showed vasodilatation Twelve patients were relieved by preganglionic sympathectomy of the limb, 1 was cured by artificial-fever therapy, and 2 recovered spontaneously The authors state that the personality changes that are always present during the painful stages were due to the patients' reaction to the pain All the patients were classified as normal and with a stable personality when examined by psychiatrists after they had been relieved of the pain

RUPTURED INTERVERTEBRAL DISKS

Lumbar Disks

Mixter and Barr in 1934 elaborated the clinical syndrome of protruded intervertebral disk in the lumbar region Since that time many cases of this

syndrome have been recognized, and in the literature of the past year a number of articles have appeared that summarize the present status of the subject The significant diagnostic features are outlined, and the results obtained with operative and nonoperative treatment are reported

The diagnosis of ruptured disk is discussed by Munro¹⁹ and by Poppen²⁰ They agree that, although this diagnosis can be made in the lumbar region on the basis of a typical history and characteristic physical findings in a large percentage of cases, the use of a contrast media to visualize the subarachnoid space is often necessary, not only for diagnosis but also for accurate localization of the protruded disk or disks An increase in the protein content of the cerebrospinal fluid was found in less than 50 per cent of the cases of both these writers They each conclude that the examination of the cerebrospinal fluid is not of great value in the diagnosis Love,²¹ however, in discussing the differential diagnosis of ruptured disk and spinal-cord tumor states that the finding of a protein content greater than 100 mg per 100 cc is in favor of the diagnosis of tumor

Attention is called by French and Payne²² to the fact that ruptured disks may be large enough to compress the entire cauda equina, and to produce complete or incomplete subarachnoid block They report 8 such cases in which the differential diagnosis from a neoplasm of the cauda equina was almost impossible A similar case was reported by Munro¹⁹

The results of treatment, both surgical and non-surgical, are reported by Grant,²³ Poppen,²⁰ Shinnars and Hamby,²⁴ and Botterell, Keith and Stewart.²⁵ Grant²³ gives the results obtained in 150 patients who were operated on and in 93 treated by conservative measures — rest in bed, leg traction and so forth In 48 per cent of the cases, operation was followed by complete relief of symptoms, in 41 per cent, the patients were improved but still experienced some pain and their work ability was below normal, and in 11 per cent, there was no relief Conservative treatment resulted in complete recovery in 21 (37 per cent) of 57 patients who were bedridden or unable to work, and in partial recovery in 27 (47 per cent) Grant concludes that surgery is not the only possible treatment for ruptured intervertebral disk, since many patients recover with rest, leg traction, back support or other nonoperative means If these measures are not successful, he adds, surgery should be considered

Shinnars and Hamby²⁴ surveyed the results in 87 patients subjected to operation, of whom 63 were private patients and 24 were industrial-compensation cases The results were approximately equal in both groups Relief of symptoms was obtained in 41 per cent of the latter group and in 52 per cent of the former In the remainder of the patients

ing patients, 3 were well, 5 were considerably improved, 5 were moderately improved, and 3 showed no improvement. A thymic tumor was present in only 2 cases. In Viets's series of 15 cases, a thymic tumor was present in 4 patients. The clinical results in 12 patients of this series observed for some months were operative death in 4, complete remission in 2, distinct improvement in 2, moderate improvement in 3 and slight improvement in 1. Favorable results, when they occurred, were not related to the presence of hyperplasia of the thymic gland. The role of this gland in myasthenia gravis is still not settled, and its removal is not recommended by Viets for patients whose symptoms are well controlled by a moderate amount of neostigmine or for those over fifty years of age.

The constancy of ocular signs in myasthenia gravis is stressed by Walsh.⁴⁸ Ptosis, weakness of the orbicularis oculis or limitation of the ocular movements unilaterally or bilaterally was found in all of 63 cases examined at the Johns Hopkins Hospital. They usually appeared early in the course of the disease but were occasionally a late development. Pupillary abnormalities did not occur.

VASCULAR LESIONS OF THE NERVOUS SYSTEM

Attention is called by Scheinker⁴⁹ and Malamud⁵⁰ to the fact that the nervous system may be involved in thromboangitis obliterans and periarteritis nodosa. Scheinker states that the early symptoms may be due to reversible circulatory disturbances (angiospasm and vasoparalysis). If these disturbances are prolonged or of repeated occurrence, irreversible changes are produced in the parenchyma. The histologic criteria for the differential diagnosis of the two conditions are given in detail.

Taylor and Page⁵¹ analyzed the records of 40 patients who died with essential hypertension in an attempt to determine whether any of the clinical features had made it possible to predict that cerebral apoplexy would occur. Among the 19 cases with a fatal cerebral hemorrhage, five symptoms were consistently observed, these were severe occipital and nuchal headache, vertigo or syncope, motor or sensory neurologic disturbances, nosebleeds and retinal hemorrhages in the absence of papilledema or exudate. These findings were negligible or absent among those patients who died of other causes.

Loman and Dameshek⁵² report a case of severe secondary polycythemia with increased intracranial pressure, choked disks and amblyopia in which there was a dissociation between an increased internal pressure in the jugular vein and a normal general venous pressure. The authors conclude that the increased venous pressure in the head and the increased intracranial pressure were due to simple plethora of the intracranial venous system. Venesection resulted

in reduction of both pressures, as well as a subsidence of the choked disks.

Weisman and Adams⁵³ review the neurologic complications of dissecting aortic aneurysm and report the findings in 11 cases from the Boston City Hospital. The clinical syndromes were divided into the following groups: ischemic necrosis of the peripheral nerves, due to extension of the dissection into a major artery of an extremity, with flaccid paralysis and anesthesia of the involved extremity, ischemic necrosis of the spinal cord, resulting from occlusion of the intercostal and lumbar arteries, with flaccid paralysis, anesthesia and sphincter disturbances below the level of the necrosis, and ischemic necrosis of the brain following extension of the dissection of the aneurysm into the carotid or innominate arteries. In some such cases there was confusion, coma, hemiplegia, hemianesthesia or aphasia.

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chitis and epididymitis — were not influenced by the treatment, nor was the acute fibrinous pericarditis present in 1 case

Meads, Harris, Samper and Finland³⁶ report 9 cases of meningococcal meningitis treated intraspinously and intramuscularly with penicillin at the Boston City Hospital, with recovery in all cases. In 2 cases, because of poor clinical response and persistence of abnormal bacteriologic and spinal-fluid chemical findings, the penicillin was discontinued and sulfapyrazine was given parenterally and orally. In 1 case, because of persistently positive throat cultures after one week of penicillin therapy, a forty-eight-hour course of sulfadiazine was given orally. The authors conclude that the clinical and laboratory findings in their 9 cases, when viewed in the light of accumulated results of sulfonamide therapy, suggest that in the treatment of Group I meningococcus meningitis the sulfonamides are the drugs of choice. Penicillin may be effective in the doses used, but the response is less favorable than that from sulfonamide therapy.

At the present time the sulfonamides (sulfadiazine) seem to give better results in the treatment of meningococcal meningitis than does penicillin. The 9 per cent mortality rate in 117 penicillin-treated cases reported in the literature is higher than that for any series of cases treated with sulfadiazine. There are, however, reports of cures by penicillin after sulfonamides had failed.

Penicillin has been effective in decreasing the mortality rate in pneumococcal meningitis. In 53 cases reported by various authors³²⁻³⁹ there were 15 deaths, a mortality rate of 28 per cent. Most of the workers agree that the sulfonamides should be used in conjunction with penicillin.

Cavernous Sinus Thrombosis

Cure of single cases of cavernous sinus thrombosis with the administration of penicillin are reported by Nicholson and Anderson,⁴⁰ Goodhill,⁴¹ and Harford, Martin, Hageman and Wood.³⁹ Sulfonamide drugs had been ineffective in all 3 cases.

Syphilis

The value of penicillin in the treatment of syphilis of the nervous system cannot be determined from the reports in the literature. Only a small number of cases have been treated, and none have been followed for a sufficiently long interval to determine the final results. The evaluation of results is further complicated by the fact that many workers do not feel justified in withholding other forms of therapy while giving penicillin. It has been shown, however, by Nelson and Duncan⁴² that in cases of acute syphilitic meningitis the intramuscular injection of penicillin in dosages varying from 600,000 to 4,000,000 units was effective in relieving the symptoms and in producing improvement in the abnormalities in the cerebrospinal fluid.

Stokes and his collaborators⁴³ report beneficial effects on the clinical course and the cerebrospinal-fluid abnormalities in patients with dementia paralytica, tabes dorsalis, optic atrophy and other forms of neurosyphilis. The total number of cases in each of the categories was small, and the period of observation was not sufficient for one to draw any definite conclusions regarding the comparative value of penicillin and previous modes of therapy.

Goldman⁴⁴ treated 18 patients with dementia paralytica with penicillin. Seven were given fever therapy and penicillin intramuscularly. The clinical results obtained did not differ significantly from those previously reported in the literature for fever therapy alone. Eleven patients were treated with intraspinous and intramuscular injections of penicillin alone. Two of these were in poor condition and died within ten days of admission to the hospital. There was some degree of improvement in the remaining 9 patients.

Neymann, Heilbrunn and Youmans⁴⁵ treated 5 cases of dementia paralytica with penicillin by various routes because intravenous and intramuscular injections did not pass the hematoencephalic barrier. They found that the administration of the drug by intracisternal injections in amounts greater than 30,000 units was unsafe because of convulsive seizures and meningeal irritation. Two such patients lapsed into coma and died after the injections. These authors state that the chronic pachymeningitis and leptomeningitis were favorably influenced by the drug, but that the syphilitic involvement of the parenchyma in the depths of the cortex probably remained unchanged.

MYASTHENIA GRAVIS

Neostigmine has been used in the treatment of myasthenia gravis for the last ten years. The results obtained with the use of this drug on 125 patients at the Massachusetts General Hospital since its introduction are presented by Viets.^{46, 46} The theory of the mode of action of the drug is that it allows acetyl choline to remain at the myoneural junction, thus forming the connecting link between the nerve impulse and the muscle. According to Viets, the amount of neostigmine to be administered daily should be sufficient to make the transmission of the impulse efficient. The daily oral dose varies from a few milligrams to an intake as high as 31 mg given in hourly doses, throughout the day and night. The drug can be administered intravenously. Potassium chloride and ephedrine sulfate can be used as adjuvants. Guanidine hydrochloride, although effective in some cases, is not favored by Viets because of the untoward side symptoms, consisting of paresthesias around the mouth and at the fingertips. The role of the thymic gland in the etiology of myasthenia gravis is considered by Blalock⁴⁷ and Viets.⁴⁸ The gland was removed from 20 patients by Blalock. Four patients died. Of the 16 remain-

ing patients, 3 were well, 5 were considerably improved, 5 were moderately improved, and 3 showed no improvement. A thymic tumor was present in only 2 cases. In Viets's series of 15 cases, a thymic tumor was present in 4 patients. The clinical results in 12 patients of this series observed for some months were operative death in 4, complete remission in 2, distinct improvement in 2, moderate improvement in 3 and slight improvement in 1. Favorable results, when they occurred, were not related to the presence of hyperplasia of the thymic gland. The role of this gland in myasthenia gravis is still not settled, and its removal is not recommended by Viets for patients whose symptoms are well controlled by a moderate amount of neostigmine or for those over fifty years of age.

The constancy of ocular signs in myasthenia gravis is stressed by Walsh.⁴⁸ Ptosis, weakness of the orbicularis oculis or limitation of the ocular movements unilaterally or bilaterally was found in all of 63 cases examined at the Johns Hopkins Hospital. They usually appeared early in the course of the disease but were occasionally a late development. Pupillary abnormalities did not occur.

VASCULAR LESIONS OF THE NERVOUS SYSTEM

Attention is called by Scheinker⁴⁹ and Malamud⁵⁰ to the fact that the nervous system may be involved in thromboangitis obliterans and periarteritis nodosa. Scheinker states that the early symptoms may be due to reversible circulatory disturbances (angiospasm and vasoparalysis). If these disturbances are prolonged or of repeated occurrence, irreversible changes are produced in the parenchyma. The histologic criteria for the differential diagnosis of the two conditions are given in detail.

Taylor and Page⁵¹ analyzed the records of 40 patients who died with essential hypertension in an attempt to determine whether any of the clinical features had made it possible to predict that cerebral apoplexy would occur. Among the 19 cases with a fatal cerebral hemorrhage, five symptoms were consistently observed, these were severe occipital and nuchal headache, vertigo or syncope, motor or sensory neurologic disturbances, nosebleeds and retinal hemorrhages in the absence of papilledema or exudate. These findings were negligible or absent among those patients who died of other causes.

Loman and Dameshek⁵² report a case of severe secondary polycythemia with increased intracranial pressure, choked disks and amblyopia in which there was a dissociation between an increased internal pressure in the jugular vein and a normal general venous pressure. The authors conclude that the increased venous pressure in the head and the increased intracranial pressure were due to simple plethora of the intracranial venous system. Venesection resulted

in reduction of both pressures, as well as a subsidence of the choked disks.

Weisman and Adams⁵³ review the neurologic complications of dissecting aortic aneurysm and report the findings in 11 cases from the Boston City Hospital. The clinical syndromes were divided into the following groups: ischemic necrosis of the peripheral nerves, due to extension of the dissection into a major artery of an extremity, with flaccid paralysis and anesthesia of the involved extremity; ischemic necrosis of the spinal cord, resulting from occlusion of the intercostal and lumbar arteries, with flaccid paralysis, anesthesia and sphincter disturbances below the level of the necrosis, and ischemic necrosis of the brain following extension of the dissection of the aneurysm into the carotid or innominate arteries. In some such cases there was confusion, coma, hemiplegia, hemianesthesia or aphasia.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 31351

PRESENTATION OF CASE

A forty-nine-year-old man was admitted to the hospital complaining of recurrent respiratory infections.

Twelve years before admission he contracted lobar pneumonia, due to a Type 1 pneumococcus. The following year he had another attack, due to a Type 4 pneumococcus. A few months later he again had pneumonia, from which he recovered slowly. One year before admission he suffered two severe attacks of bronchitis, with a cough productive of white or yellow sputum. At times the sputum was malodorous, and on one occasion it contained a small clot of blood. There was no pleurisy or night sweats. Lying on his left side caused severe coughing. Six months before admission, bronchitis recurred and persisted. During this episode he coughed up a great deal of malodorous sputum. The patient became extremely weak and was confined to bed. Two months later, an x-ray film of the chest revealed enlarged hilar nodes, these did not respond to x-ray

therapy. A later film was said to have demonstrated a fluid level. A month before admission he underwent a course of penicillin, following which he became symptom-free.

The past history was noncontributory.

Physical examination revealed a well developed and well nourished man in no acute distress, no outstanding abnormalities were noted.

The temperature was 98°F, the pulse 80, and the respirations 20. The blood pressure was 135 systolic, 95 diastolic.

Examination of the blood showed a white-cell count of 6600, with 66 per cent neutrophils. The hemoglobin was 13.6 gm. The nonprotein nitrogen was 22 mg per 100 cc. A blood Hinton test was negative. The urine was normal.

A chest plate showed a sharply circumscribed mass, approximately 10 cm in diameter, that appeared to rise from the mediastinum (Fig. 1). It moved upward with swallowing, and in its upper portion there was a fluid level. There were no areas of calcification in the mass. There was no interference with aeration of the various lobes. Both halves of the diaphragm were smooth in outline and showed normal motion. The lung fields were clear. There was no evidence of metastases in the visible bones. The mass displaced the esophagus slightly to the left.

On the third hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. HELEN S. PITTMAN. We might start by seeing the x-ray films.

DR. MILFORD D. SCHULZ. Here is a large mass overlying the right border of the heart and the first portion of the aorta. It is smooth in outline and seems to lie in the central portion of the right chest

*On leave of absence.

It contains a fluid level. This, together with the fact that it was reported to move on swallowing, makes one think it had something to do with the respiratory tree. The mass does not seem to have caused a great deal of compression on the lung.

DR. PITTMAN: This seems like a simple, straightforward problem. I have gone over it trying to make it complicated but have not been able to do so. I think that this mediastinal mass was a bronchial cyst, with bronchial communication and recurrent

the organisms that one expects to cause a lung abscess and since this mass does not seem to be out in the lung tissue, the possibility of its representing an old abscess is so remote that I shall pay no attention to it.

A smooth mass in this position is what one finds in a cyst, and I am not going through the differential of all the tumors that could be found here. The history is perfectly characteristic of infection with bronchial plugging, subsequent release of the bron-

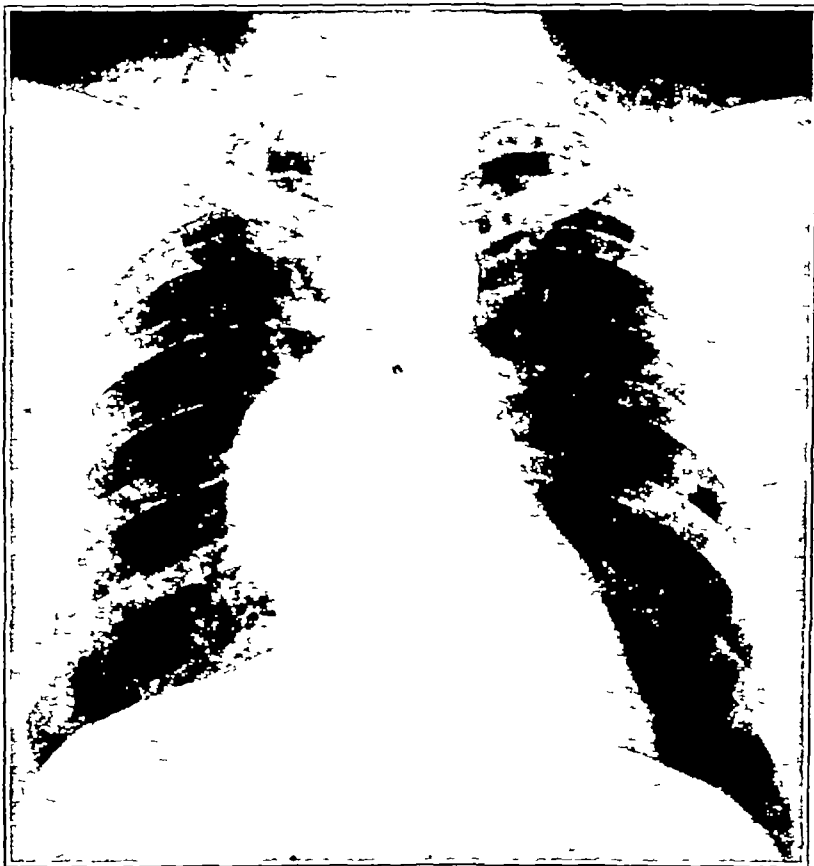


FIGURE 1

infection. I shall try to break that down briefly, but I cannot see anything else for it to be.

There was a history going back twelve years. In many cases of chronic bronchopulmonary infection the history of recurrent pneumonia is important. In this patient I do not believe that it is, although he had had three attacks of pneumonia years ago. When talking about bronchial cysts, one has to consider whether they arise in the lung or in the mediastinum, and often one cannot be perfectly sure which is the case.

A cystic mass in the lung may be a burned-out abscess, one with free bronchial communication and which therefore does not produce much surrounding pneumonitis. Since pneumococci are not

chial obstruction and the liberation of large amounts of foul, stinking sputum. There was no calcification in the mass, which argues against a dermoid cyst or tuberculoma, and one is much less likely to find this story of infection and sputum with them.

I think that a diagnosis of bronchial cyst was made and that the patient was sent in for operation. On the outside he was said to have had hilar nodes. I assume that the cyst had been interpreted as a mass of hilar nodes, and since one may not be able to tell by x-ray appearance the difference between a benign and a malignant tumor, it was perfectly proper to give a course of x-ray therapy to see what happened.

My diagnosis is mediastinal cyst arising from the

bronchial or tracheal wall. The fact that it moved with swallowing suggests that it was close to the trachea or to the carina. I believe that there was a bronchial communication and that there has been recurrent infection in the cyst. It was probably on a congenital basis, as most of these are, undoubtedly the operation was complete excision of the cyst.

CLINICAL DIAGNOSIS

Bronchiogenic cyst

DR PITTMAN'S DIAGNOSIS

Mediastinal cyst arising from bronchus

ANATOMICAL DIAGNOSIS

Congenital mediastinal cyst arising from esophagus

PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMAN I am sorry that Dr Richard H Sweet is not here. I shall read portions of his operative note.

The tumor was found to be a cystic one presenting posteriorly to the lung and extending upward behind the right main bronchus a short way and pushing the azygos vein up. It was densely adherent to the lung and also to all the adjacent structures, including the esophagus and the pericardium. The dense adhesions were undoubtedly the result of the infection that he had had early this year.

An incision was made through the overlying pleura, and dissection was first carried posteriorly, freeing the azygos vein and the esophagus from the tumor. The esophagus was quite adherent, but it was relatively easy to dissect it free except at one point where there was a tenting up of the esophagus with what appeared to be a band-like structure going directly into the wall of the cyst, which was extremely thick. This adherent portion was left until a later stage of the operation, and the dissection was then carried around with great difficulty posteriorly and downward on the medial side, freeing the mass from the bronchus. In doing this it was discovered that the cyst had to be freed from the medial surface of the left main bronchus as well as from the carina and the right main bronchus. There was no plane of cleavage and all the dissection had to be done by cutting blindly. The anesthetist had great difficulty because the patient's mouth kept filling up with the foul-smelling contents of the cyst. The amount of the material that accumulated in the throat gradually assumed alarming proportions, and the patient became quite cyanotic. Something drastic had to be done. An incision was therefore made in the wall of the cyst, and the remainder of the contents was removed by aspiration. This immediately stopped the difficulty, and after all the fluid from the throat and trachea had been aspirated there was no further trouble of that nature. The opening of the cyst facilitated its removal, because it was then possible to palpate from within and see where it was necessary to cut in order to separate it from the lung and the remaining portion of the bronchi. The adhesions to the pericardium were very dense, but the cyst was finally removed from the wall of the pericardium without cutting into the latter. It finally became necessary to separate the small bridge of tissue that connected the cyst with the esophagus, and in cutting across this there was a definite channel between the cyst and the esophagus about 4 mm in diameter. This was obviously the point of escape of the cyst contents. There was no communication between the cyst and any portion of the bronchi at tree. The cyst was finally removed without the necessity of doing a lobectomy.

When we received the cyst we observed, of course, all the adhesive bands of connective tissue around

it. The contents had been aspirated, and the inner lining of the cyst had a thick, pebbly, leathery appearance, simulating leukoplakia of the esophagus. The sections showed microscopically that this cyst was lined with a thick layer of stratified squamous epithelium, such as one sees in the esophagus. Beneath the epithelium were glands such as are found in the esophagus, but there was no muscle tissue. In other words, it was made up of a thick layer of connective tissue with an esophageal lining. I felt sure that this was not a true bronchial cyst, because they are lined with respiratory epithelium. I thought of a duplication of the esophagus, such as has been described in children by Ladd and Gross¹ and has been recently explained embryologically by Dr J Lewis Bremer,² but the absence of smooth muscle in the wall of the cyst rules this out. I have asked Dr Bremer of the Department of Anatomy, Harvard Medical School, to come down here today to tell us something about the embryology of this cyst.

DR J LEWIS BREMER I believe that this case just missed being one of tracheoesophageal fistula. If you recall the story of tracheoesophageal fistula, you will remember that the pharynx curves down from the mouth and is provided with four paired lateral pouches or outgrowths. Just below the last pair is another double outgrowth from the ventral surface, this is to become the lungs (Fig 2a)

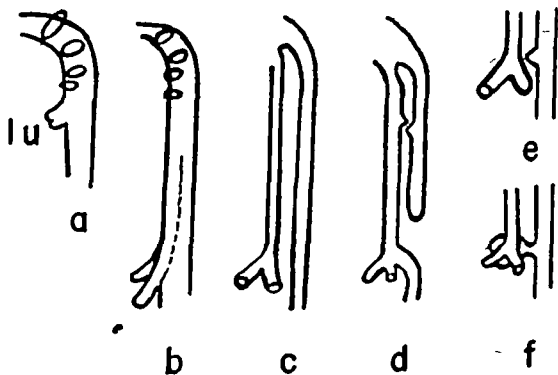


FIGURE 2

The heart lies at first in the curve of the pharynx, and as it descends the lung bud is drawn down with it. The pharynx between it and the lowest pouches is thereby elongated enormously (Fig 2b). This takes place very early, about the fourth week. The lengthened part of the pharynx becomes flattened laterally, the two lateral walls finally fusing, thus dividing the single pharynx into two tubes, the trachea in front and the esophagus behind. The process begins at the lung bud and proceeds upward (Fig 2c). The trachea does not grow out like the duct of an ordinary gland, but is really part of the esophagus. The only derivatives of the lung bud are the bronchi and lungs.

Normally the separation is complete. Occasionally it is incomplete, with connection between the two tubes at one or more places. Most often the connection is at the lower end near the original lung bud (Fig 2*d*). The esophagus is usually interrupted just above the connection. This is the usual form of tracheoesophageal fistula. Often in these cases there may be at a higher level small tent-shaped pockets from both trachea and esophagus, not meeting each other, but looking as though they had just broken apart. These are traction diverticula. I think that the present case represents a traction diverticulum of the esophagus in the region of and replacing the usual tracheoesophageal fistula (Fig 2*e*). It has swollen up as a large cyst with a narrow stalk and has adhered to the bifurcation of the trachea and to both bronchi (Fig 2*f*).

There was no muscle in the wall of this cyst. The reason for this is that it originated before muscle is present in the esophagus. Muscle develops only where it is needed, as in swallowing, but in a side pocket like this cyst there is no such necessity. Foul-smelling material was brought up with coughing. In coughing the whole chest is compressed, including the mediastinum and, in this case, the cyst, and its contents of foul-smelling retained food escaped through the esophagus.

I have never seen such a case before, but I imagine that this is the explanation of it.

DR. RODOLFO E. HERRERA: Was there any cartilage?

DR. BREMER: There should not be.

DR. LEROY A. SCHALL: No muscularis mucosa.

DR. CASTLEMAN: It consisted of epithelium and connective tissue, in the submucosa there were mucous glands. There was, of course, evidence of long-standing infection.

DR. BREMER: One always finds lymphocytes around the ducts of the tracheal glands.

DR. CASTLEMAN: I suppose this could be called a congenital esophageal cyst for the same reason that a congenital cyst arising from the bronchus is called a bronchiogenic cyst.

The patient did well postoperatively and was discharged in three weeks.

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CASE 31352

PRESENTATION OF CASE

A sixty-four-year-old man was admitted to the hospital complaining of back pain.

Seven weeks before admission he suddenly developed severe pain in the lower thoracic spine, which radiated anteriorly to the front of the chest. Analgesics gave no relief. A week later he

went to a community hospital, where the pain was controlled by narcotics. It gradually subsided over a period of several weeks. He rapidly lost strength in his lower extremities, however, and a week after entering the hospital he was unable to walk. On admission to this hospital he was still able to move his legs. During the period of his illness he was compelled for the first time to strain in order to void.

The past history was noncontributory.

The patient was a well developed and well nourished man in no acute distress. The pupils reacted to light and accommodation. The chest was barrel-shaped. The prostate was normal. Pain and touch sensibility was diminished below the seventh thoracic segment, and sensation of position was absent in the feet. The arm, knee, and ankle jerks were present and equal, the abdominal reflexes were absent, and the plantar reflexes doubtful.

The temperature was 99°F, the pulse 90, and the respirations 20. The blood pressure was 100 systolic, 70 diastolic.

On entry, the urine was normal, containing no Bence-Jones protein. Succeeding urine specimens gave + to ++ tests for albumin. The red-cell count was 4,300,000 with a hemoglobin of 80 per cent, and the white-cell count 8000, with 60 per cent neutrophils, 29 per cent lymphocytes, 5 per cent monocytes and 2 per cent eosinophils. Gastric analysis showed 100 units of free hydrochloric acid after 1 mg of histamine. The stools were guaiac negative. A rapid Hinton test was negative. The nonprotein nitrogen was 38 mg per 100 cc, the total protein 7.1 gm, the fasting blood sugar 105 mg, the serum phosphorus 2.8 mg, the alkaline phosphatase 5.2 units, and the acid phosphatase 1.4 units.

X-ray films taken soon after admission showed decalcification of the left pedicle of the sixth thoracic vertebra. The lungs were clear, and the heart was not remarkable. A myelogram was attempted but was unsuccessful. Two weeks later, however, x-ray films showed considerable narrowing of the disk space between the fifth and sixth thoracic vertebrae. The right pedicle of the sixth thoracic vertebra was partially destroyed, and there was a defect of the right lateral portion of the body of this vertebra. Lumbar puncture shortly after admission yielded clear fluid under a pressure equivalent to 90 mm of water. Jugular compression did not cause any rise in pressure, with abdominal compression it rose to 250 mm. No cells were seen. The protein content was 114 mg per 100 cc, and the Wassermann was negative.

A week after admission sensory impairment had become more pronounced but the level remained unchanged. There was complete paralysis of the legs. The knee and ankle jerks were absent. The plantar reflexes were not extensor. The patient had increasing difficulty voiding and was placed on closed bladder drainage. An operation was performed on the sixteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR ARTHUR L. WATKINS We have a story of only seven weeks' duration, beginning with backache and pain radiating anteriorly, which suggests spinal-root involvement. The simplest explanation might be arthritis, a mechanical back disturbance of some sort, herpes zoster or intercostal neuralgia. But all these are rather easily ruled out by the onset within a week of signs suggesting involvement of the spinal cord, with presumable compression. There was a definite sensory level, and progressive weakness of the legs. Also, lumbar puncture later showed signs of block. So far as localization is concerned, the symptoms suggest a lesion that is compressing the spinal cord at the level of the sixth or seventh thoracic segment, and the x-ray studies give a further lead. We might see the films now.

DR MILFORD D. SCHULZ The pedicles of the sixth segment on the left are decalcified. There is some narrowing of the intervertebral space between the sixth and the fifth segments. Whether that is associated with the lesion or due to something that existed previously, I do not know.

DR WATKINS The report mentioned a later film showing a change in that respect.

DR CHARLES S. KUBIK Also, that the spine showed destruction laterally.

DR SCHULZ I do not see a great deal of change in the second set of films. I wonder whether the appearance of destruction on the lateral surface of this segment may not have been due to rotation rather than actual destruction of bone. No, on looking at it more closely I believe that there is definite destruction: the left side of the sixth body does not seem to be so well formed as the segments above and below.

DR WATKINS There is no widening of the interpedicular space?

DR SCHULZ That is difficult to say without measuring and comparing them to standard curves, but I do not believe there is appreciable widening of the interpediculate spaces.

DR KUBIK Is there any soft-tissue mass?

DR SCHULZ I can see none.

DR WATKINS And no calcification?

DR SCHULZ No. The only definite change is the apparent destruction of the pedicle.

DR WATKINS We have then, with the help of the x-ray films, further confirmation of a lesion that seems to have been at the level of the sixth thoracic vertebra. It might have been due to a ruptured disk, but there does not seem to be much to favor that, although there is some narrowing of the disk space. One would not expect to find decalcification of the vertebra and the pedicle.

So far as infectious processes are concerned, we know that an epidural abscess can give a sudden transverse myelitis, but the course here was rapidly progressive. There were no cells in the spinal fluid, no local tenderness, and no general signs of an in-

fectious process. In tuberculosis of the spine one would not expect to have such a rapid progression of neurologic signs without evidence of more extensive bone destruction, possibly with soft-tissue changes, than is apparent in this case.

I suppose that this could have been a gumma. There is no hint, however, that the patient had ever had syphilis. I presume that the decalcification could have been simply due to pressure from a tumor, with some pulsation from below transmitted to it. I do not know how we can make a diagnosis of gumma. The x-ray studies do not give any lead, and although I cannot rule it out, I shall have to say that there is no evidence for it.

As for vascular lesions, hematomyelia can give neurologic symptoms, but one would expect dissociated sensory loss, without evidence of block or of a destructive lesion in the vertebra. As for other intrinsic cord diseases, multiple sclerosis, central-nervous-system syphilis, syringomyelia and other degenerative lesions can be ruled out because of the block, and the symptoms are in no way suggestive.

So we are left with a diagnosis of tumor. Could it have been an intramedullary tumor? The first symptoms were those of root involvement, and this is much against a primary intramedullary tumor, such as a glioma. The early appearance of bone changes and the rather rapid course are also against that diagnosis. The most frequent tumors involving the spinal cord are the extramedullary intradural tumors, and among these, a meningioma is probably of commonest occurrence. The history is consistent with an extramedullary intradural tumor, since the symptoms began with root pain and the rapid onset of neurologic signs. Perhaps first there may have been some evidence of spasticity, we do not know how lively the reflexes were. There may have been a Babinski sign, and the abdominal reflexes were absent. We do not know how the legs felt: whether they seemed to be hypertonic or whether there was, instead, a rather rapid development of a flaccid type of paralysis, which would be consistent with fairly rapidly progressing compression by a tumor situated in this position. Most of the extramedullary extradural tumors give similar clinical symptoms, and it would be difficult to differentiate them in this case.

It may have been a metastatic lesion, but we do not have any evidence of a primary site. There was free acid in the stomach, and the stool was guaiac negative. So we have nothing suggesting that there was anything wrong in the gastrointestinal tract. The prostate was described as normal. There is a possibility that a renal-cell tumor had metastasized to the spine, — a solitary metastasis, — but we have no evidence of a mass in the kidney region. Some albumin was found in the urine, and there was slight anemia. Against metastatic disease are the normal phosphatase and the fact that the lesion

was small and focal, without evidence of diffuse bone involvement

Among the bone tumors we must consider multiple myeloma — in this case, I suppose, a single myeloma. There was, however, no Bence-Jones protein, and one would not expect to find such a rapid progression of neurologic signs without more evidence of bone involvement. As for hemangioma, these tumors are likelier to cause a more specific x-ray appearance. The rather rapid course, only six weeks, is against a hemangioma. Osteogenic sarcoma would tend to give evidence of extensive bone disease before showing this degree of neurologic involvement.

So this brings us to a primary tumor, either benign or malignant. The most frequent benign lesion is meningioma. Sometimes calcification in the x-ray films gives a lead. A neurofibroma can give a similar appearance. If the tumor was responsible for the narrowing of the disk space, it probably was not a meningioma or neurofibroma. This would suggest a more destructive or invasive tumor, possibly an epidural sarcoma. I do not know, however, whether we can be sure that the narrowing of the disk space was related to the process, it may have been due to an old injury. In this location, narrowing of the intervertebral space is fairly frequent. The report suggests that the narrowing had increased during the hospital stay, but I gather that that is not particularly evident from the x-ray films.

Rare conditions such as dermoid tumors and Hodgkin's disease involving bone seem unlikely. There was no soft-tissue involvement or enlarged lymph nodes in the mediastinum. There was no calcification suggesting dermoid, and the process does not seem to have been as extensive as one would expect in that condition. It could have been a lipoma, but these lesions are likely to be multiple. We do not know how far it extended, but so far as one can tell from the x-ray appearance, it was fairly well localized. I cannot rule out lipoma, but it seems less likely than a meningioma or neurofibroma.

On the law of chances, which one cannot count on too much at these exercises, I am going to conclude that there was a lesion compressing the spinal cord at the level of the sixth thoracic vertebra, presumably a tumor. It was probably extramedullary, and it probably arose in this region, either a meningioma or a neurofibroma, but the rapid course suggests that it may have been a primary epidural sarcoma.

DR JOST MICHELSEN I should like to know more about the urine examinations.

DR KUBIK The sediment contained 5 to 25 white cells and 4 red cells per high-power field, and on one examination there were a few epithelial cells.

DR MICHELSEN There was no urinary infection?

DR KUBIK No cultures were taken.

DR MICHELSEN Does Dr Watkins attach any significance to the albumin?

DR WATKINS It might make one think of hypernephroma. It was the only lead I had.

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DR SCHULZ, can you make a diagnosis from the x-ray films?

DR SCHULZ I am sure that I do not know what it is.

DR WILLIAM SWEET I have seen one patient who had a rapidly developing erosion of the pedicle from a rare condition that Dr Watkins did not mention — a neurofibrosarcoma. The tumor arose in the nerve root. When I removed the intraspinal portion of the lesion, I thought that it was a benign tumor. It extended through the intervertebral foramen, and the thoracic surgeon later removed the intrathoracic portion. The intraspinal portion looked benign microscopically, but the intrathoracic portion contained innumerable mitotic figures. The patient subsequently succumbed.

DR KUBIK It was probably a benign tumor that had become malignant.

CLINICAL DIAGNOSIS

Metastatic carcinoma

DR WATKINS'S DIAGNOSES

Spinal-cord compression by tumor at level of sixth thoracic vertebra

Epidural sarcoma?

Meningioma or neurofibroma?

ANATOMICAL DIAGNOSIS

Tuberculosis of vertebra, with extension to dura.

PATHOLOGICAL DISCUSSION

DR KUBIK The Neurosurgical Service suspected that this man had metastatic malignancy, but the possibility of tuberculosis was mentioned once. The X-ray Department favored malignant tumor, either metastatic carcinoma or lymphoma.

When the region was explored, reddish tissue outside the dura, which was thought to be tumor, was found under the sixth dorsal nerve root. The entire lateral wall of the spinal canal was removed, exposing the nerve root in its canal and the tumor over a distance of almost 4 cm. No definite destruction of the vertebral bodies was seen during the removal of pieces of the tumor. The tumor had a dumbbell extension alongside the root through the foramen, and with suction, gelatinous whitish tissue somewhat suggestive of tuberculosis was removed. The dura was not opened.

Microscopical examination showed the mass to be a tuberculous epidural process, presumably extending from tuberculosis of the vertebra, although this was not observed at operation.

DIFFERENTIAL DIAGNOSIS

DR ARTHUR L. WATKINS We have a story of only seven weeks' duration, beginning with backache and pain radiating anteriorly, which suggests spinal-root involvement. The simplest explanation might be arthritis, a mechanical back disturbance of some sort, herpes zoster or intercostal neuralgia. But all these are rather easily ruled out by the onset within a week of signs suggesting involvement of the spinal cord, with presumable compression. There was a definite sensory level, and progressive weakness of the legs. Also, lumbar puncture later showed signs of block. So far as localization is concerned, the symptoms suggest a lesion that is compressing the spinal cord at the level of the sixth or seventh thoracic segment, and the x-ray studies give a further lead. We might see the films now.

DR MILFORD D. SCHULZ The pedicles of the sixth segment on the left are decalcified. There is some narrowing of the intervertebral space between the sixth and the fifth segments. Whether that is associated with the lesion or due to something that existed previously, I do not know.

DR WATKINS The report mentioned a later film showing a change in that respect.

DR CHARLES S. KUBIK Also, that the spine showed destruction laterally.

DR SCHULZ I do not see a great deal of change in the second set of films. I wonder whether the appearance of destruction on the lateral surface of this segment may not have been due to rotation rather than actual destruction of bone. No, on looking at it more closely I believe that there is definite destruction. The left side of the sixth body does not seem to be so well formed as the segments above and below.

DR WATKINS There is no widening of the interpedicular space?

DR SCHULZ That is difficult to say without measuring and comparing them to standard curves, but I do not believe there is appreciable widening of the interpediculate spaces.

DR KUBIK Is there any soft-tissue mass?

DR SCHULZ I can see none.

DR WATKINS And no calcification?

DR SCHULZ No. The only definite change is the apparent destruction of the pedicle.

DR WATKINS We have then, with the help of the x-ray films, further confirmation of a lesion that seems to have been at the level of the sixth thoracic vertebra. It might have been due to a ruptured disk, but there does not seem to be much to favor that, although there is some narrowing of the disk space. One would not expect to find decalcification of the vertebra and the pedicle.

So far as infectious processes are concerned, we know that an epidural abscess can give a sudden transverse myelitis, but the course here was rapidly progressive. There were no cells in the spinal fluid, no local tenderness, and no general signs of an in-

fectious process. In tuberculosis of the spine one would not expect to have such a rapid progression of neurologic signs without evidence of more extensive bone destruction, possibly with soft-tissue changes, than is apparent in this case.

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"IF NOT, WHAT IS IT?"

THE following editorial, which appeared under the above heading in the August 4 issue of *The Christian Science Monitor*, clearly and ably refutes one of the arguments expounded by the sponsors of the Wagner-Murray-Dingell Bill. It is reprinted through the courtesy of the Christian Science Publishing Society

Debate has developed over whether the compulsory sickness insurance called for by the Wagner-Murray-Dingell Bill is socialized medicine. In statements given the press, sponsors of the legislation declared it "is not socialized medicine, it is not state medicine."

The bill provides for social insurance to furnish medical care, and would set up a Government system of medical service. Every eligible person who wished to receive the care offered would be limited in his choice of physician

to doctors who had signed up with the Government. If an insured worker preferred to go to some doctor outside the system, he would have to pay his insurance tax as usual and his doctor besides. Also, it is difficult to see how he could obtain the cash disability payments, making up in part for loss of wages during illness, available to those certified by Government doctors.

The doctors in the system, who according to some estimates would probably number 100,000, would be paid by the Government. They would decide for themselves whether to be paid on a fee, per capita, or salary basis, or a combination. Administration of the system would be directed by the Surgeon General of the United States Public Health Service. The confidential relationship between physician and patient would in a degree be removed by the requirement that the doctor furnish a written report to the Government on each patient and his illness.

Coverage of the plan would extend to a great percentage of the population. Most of the workers would be taxed to pay the costs through weekly pay-roll deductions. Their employers would be similarly taxed. The self-employed would also be brought in. Dependents would be included. Before many years the tax receipts would prove insufficient and, as the bill's sponsors say, the Government would have to help out with a subsidy.

Obviously, when a compulsory system of government-medical-care insurance is set up to embrace the bulk of a people, that is socialized medicine. When the Government hires doctors like postmen and pays them salaries, that is state medicine. The Wagner-Murray-Dingell Bill provides for both.

RESTRICTING THE SALE OF SULFONAMIDES

HARDLY a month has passed in recent years without the appearance in the medical literature of several reports concerning toxic manifestations in persons who took sulfonamide drugs in one form or another. Particularly disturbing are those untoward reactions that occur in persons who have previously been treated with these drugs and are later again exposed to them either through self-medication or on the advice of physicians who are unaware of the previous exposure. Apparently the nature or number of the reactions that have followed self-medication has not sufficiently impressed the proper authorities to induce them to prohibit the uncontrolled sale of sulfonamide preparations. At any rate, in most parts of this country it is still possible to purchase over the counter not only the ordinary sulfonamide tablets but also numerous other preparations, such as nose drops, adhesive-backed bandages, shaving creams and cosmetics, that contain sulfonamide drugs. Any of them may produce serious reactions in sensitized

persons, and by virtue of the fact that many of these preparations are used repeatedly, they may themselves be the cause of sensitization. A review of the dangers from the external use of sulfonamides has recently been published by the Council on Pharmacy and Chemistry of the American Medical Association.¹

Some time ago the Department of Health of the City of New York took cognizance of these dangers and forbade the sale of sulfonamide drugs for internal or external use in the form of powders, ointments or sprays without a prescription. Up to this time, however, no similar restriction has been placed on many other items, such as cosmetics, shaving creams and bandages, containing sulfonamides. The Board of Health has recently enacted an amendment to the Sanitary Code of the City of New York that restricts the dispensing of any and all kinds of preparations containing sulfonamides for internal or external use without a written prescription.² This amendment is in line with recommendations made to that board by the Public Health Relations Committee of the New York Academy of Medicine and with the expressed opinion of many of the nation's leading medical associations.

It would undoubtedly be well for other public-health authorities to follow this example. Such action, however, only emphasizes the duties of the physician in prescribing sulfonamides. He should ascertain beforehand whether the patient has previously been exposed to these drugs and whether a toxic reaction resulted from their use. He should exercise due caution in their use when he does prescribe them. Likewise, patients who have had such a reaction should be made aware of the dangers of its repetition and of the need for close medical supervision when it is necessary to give one of these drugs again. It must also be borne in mind that evidence of sensitization to a sulfonamide may not necessarily manifest itself during the first course of treatment and yet may appear in a rather violent form as soon as the drug is taken a second time. For that reason every patient should be made aware of the fact that he is taking or has taken a sulfonamide, even if no untoward effects followed its use.

REFERENCES

- 1 Dangers from external use of sulfonamides. *J A M A* 128 1024 1945
- 2 Sale of all sulfonamide products limited to "prescription only" basis. *Quart Bull., Dept of Health City of New York* 13 17 1945

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

POLIOMYELITIS AND BATHING BEACHES

Simultaneously with the report of an increase in the reported cases of poliomyelitis there arises renewed public interest in the relation of bathing beaches to the spread of the disease. When a child who has been swimming becomes infected, panic among bathers often develops and a popular demand to close the beach results.

Epidemiologists generally agree that poliomyelitis is an upper respiratory, rather than a water-borne, disease and that human contacts are responsible for its spread. For that reason the attention of the public should be directed primarily toward the avoidance of crowds in theaters, stores and other gathering places.

The department has consistently opposed the closing of approved bathing sites in Massachusetts during the period of high prevalence of poliomyelitis unless unusual circumstances exist. Moreover, the approved beaches in the Commonwealth are not located where they can be polluted by sewage. Sanitary surveys are made periodically, and the water is analyzed bacterially and chemically.

The closing of approved beaches in this state should be considered only when theaters, schools and churches are closed and all public meetings cancelled. Action of this kind is taken more frequently because the public demands it than because such closing prevents the spread of the disease.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Haverhill	September 5	William T. Green
Lowell	September 7	Albert H. Brewster
Salem	September 10*	Paul W. Hugenberger
Brockton	September 13	George W. Van Gorder
Pittsfield	September 17	Frank A. Slowick
Springfield	September 18	Garry deN. Hough, Jr.
Worcester	September 21	John W. O'Meara
Fall River	September 24	Eugene A. McCarthy
Hyannis	September 25	Paul L. Norton

*Day changed because of holiday

BOOK REVIEWS

The Art of Resuscitation. By Paluel J. Flagg, M.D. 8°, cloth, 453 pp., with 176 illustrations. New York: Reinhold Publishing Corporation, 1944. \$5.00.

This book is essentially a combination of the twenty-five years of clinical and practical experiences of the author, a review of recent military literature on asphyxia and the investigations of the Society for the Prevention of Asphyxial Death. The basis of thought is, "What is to be treated is more important than how treatment is to be applied." The frontispiece is an interesting schematic representation of the entire text.

The book is divided into seven parts. Part I deals with the definition of asphyxia, contrasting the British concept of cessation of pulse with the American concept of cessation of respiration. A brief historical background, as well as some detailed publicity for the Society for the Prevention of Asphyxial Death, is included. Part II, entitled "Asphyxia as a Generic Problem," is a sketchy review of experimental physiology and an accepted listing of the causes of asphyxia. Part III, entitled "The Principles of Resuscitation," is a discussion of the four accepted types of anoxia— anoxic, anemic, stagnant and histotoxic — and of the causes and indications for treatment. The stages of asphyxia, with their signs and symptoms, are listed. A detailed description of methods of resuscitation and an illustrative review of resuscitative apparatus are also presented. Included in this section are the modern concepts and equipment for handling and transporting unconscious patients. Part IV contains essentially the meat of the whole book. It is a detailed description and discussion of the treatment of specific types of asphyxia, listed as follows: neonatorum, high altitude, carbon monoxide poisoning, submersion, anesthesia, poliomyelitis, electrocution, fire-fighting gases, mechanical obstruction, pathologic respiratory obstruction and clinical diseases. Part V, entitled "The Field of Asphyxia and Resuscitation," covers the organization and importance, from a sociologic and economic standpoint, of the various groups, including medicine, dentistry, public health, child welfare, Army, Navy and civilian defense. In Part VI the author expounds his ideas and visions for a rebirth of the science of pneumatology. This science is built on three equally important subjects — anesthesia, resuscitation and gas therapy. Of this equilateral triangle, two books already have been published by the author — *Art of Anesthesia* and the present book.

Like *Art of Anesthesia*, this book is well written and easy to read. At times the author's interests and opinions are overly stressed and elaborated. The book contains many interesting detailed and instructive illustrations. It is an excellent reference book for information and data on resuscitation not only for physicians and dentists but also for their trained technicians.

The Etiology, Diagnosis and Treatment of Amebiasis. By Charles F. Craig, M.D. 8°, cloth, 332 pp., with 45 illustrations and 10 tables. Baltimore: Williams and Wilkins Company, 1944. \$4.50.

Dr. Craig's new book on amebiasis maintains the same high standard of excellence that he achieved in his earlier work on the same subject, entitled *Amebiasis and Amebic Dysentery*.

The two books have nearly the same number of pages, but the space devoted to the pathology of amebiasis has been considerably expanded in the new volume, and that given to some of the other subjects has been correspondingly curtailed. Because diagnosis in obscure cases depends greatly on a clear understanding of the pathologic lesions produced by amebic infection, the more complete account of the pathology is especially valuable.

The subject matter is notable for the opinions of the author, which are based on his own long experience with amebiasis. The illustrations are excellent.

The book can be highly recommended to students and to practitioners of medicine.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

The Reticulo-Endothelial System in Sulfonamide Activity. By Frank T. Maher, M.D., assistant professor of pharmacognosy and pharmacology, University of Illinois. Illinois Monographs in the Medical Sciences, Vol. V, Nos. 1-2. 4°, paper, 232 pp., with 23 illustrations. Urbana: University of Illinois Press, 1944. \$2.50 (paper bound) and \$3.00 (cloth bound).

The purpose of this monograph is to evaluate reticulo-endothelial activity in sulfonamide chemotherapy in experimental animals, and the author believes that the results presented strongly indicate its vital importance. It is his intention to continue his studies in this special field, with the hope that light will be thrown on the means by which the sulfonamide drugs accomplish their therapeutic effects. The monograph was presented in 1941 as a dissertation for the degree of philosophy in pharmacology at the Graduate School of the University of Illinois. The text is well documented, and a list of over six hundred pertinent references is appended. The book is well printed, with a good type on good paper.

A Test for Color Blindness. By P. B. Wiltberger, M.D. 12°, paper, 7 pp., illustrated. Columbus, Ohio: College Book Company, 1944. \$1.00.

This simple test claims readily to separate color blind persons from normal and color-weak persons. This new test was first published by the author in 1941. He claims that it is accurate and physiologic and cannot be memorized and that the person being tested need not be asked what color he sees and need not know the name of a single color.

NOTICES

ANNOUNCEMENT

Dr. Nathaniel M. Stone announces the removal of his office from 475 to 371 Commonwealth Avenue, Boston.

PHILLIPS SOCIETY

Dr. Eugene Kellersberger, government consultant on tropical diseases and former medical missionary to Africa, will give an illustrated lecture "Leprosy and Trypanosomiasis" at the Beth Israel Hospital amphitheater, Thursday, September 6, at 8:00 p.m. This is sponsored by the Phillips Society of Tufts College Medical School.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, September 6, in the classroom of the Nurses' Residence at 7:15 p.m. There will be a discussion of penicillin therapy with presentation of cases. Dr. Ann P. D. Manton will be chairman.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, SEPTEMBER 6

FRIDAY, SEPTEMBER 7

*9:00-10:00 a.m. Medical clinic. Isolation Amphitheater, Children's Hospital.
10:50 a.m. Allergy and Eczema Infections. Dr. John G. Downing (Postgraduate clinic in dermatology and syphilology). Amphitheater, Downing Building, Boston City Hospital.

MONDAY, SEPTEMBER 10

*12:00 m.-1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, SEPTEMBER 11

*9:00-10:00 a.m. Medical clinic. Infants' Hospital.
*12:15-1:15 p.m. Clinicorontogenetic conference. Peter Bent Brigham Hospital.

WEDNESDAY, SEPTEMBER 12

*12:00 m. Clinicopathological conference. Children's Hospital.
*12:00 m.-1:00 p.m. Clinicopathological conference. Cambridge Hospital.

*Open to the medical profession.

SEPTEMBER 6. New England Hospital for Women and Children. See notice elsewhere on this page.

SEPTEMBER 6. Phillips Society. See notice elsewhere on this page.

SEPTEMBER 13. The Hemorrhagic Diseases. Dr. William Dameshek. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

SEPTEMBER 17. American Public Health Association. Page 572, issue of November 30.

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COARCTATION OF THE AORTA*

Experimental Studies regarding Its Surgical Correction

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BOSTON

COARCTATION of the aorta is an unusual abnormality, but is found with sufficient frequency and is accompanied by severe enough complications to warrant a search for technical methods leading to its surgical correction in selected cases. Many persons with this disease have a reasonably long life and suffer relatively little incapacitation. A high degree of obstruction — or a complete block — in this arterial pathway carries a distinct hazard, however, because of the possibility of certain complications. In the first place, aneurysmal dilatation of the aorta may arise above or below the constricted zone. Secondly, a dissecting aneurysm may originate in the anomalous and sclerotic aortic wall. Thirdly, rupture of the aorta has occasionally been observed. Fourthly, *Streptococcus viridans* infection may become superimposed on the lesion. Last and most important of all, severe hypertension may develop in the upper part of the body. Following this, there may be cardiac failure, cerebral hemorrhage or other ill effects of the hypertensive state. Coarctation of the aorta usually causes few symptoms in childhood years. If important sequelae appear, they are likeliest to manifest themselves in midlife. Although some of these aortic obstructions are well tolerated for long periods, there seems to be little question that in any large series of patients the average span of life is greatly diminished below the normal expectancy.

Little attention has been given to the possibility of surgical alleviation of this congenital malformation. Perhaps experimenters have been disheartened by the great size of the blood vessels concerned and also by the inaccessibility of the structures within the mediastinum. The opening of a new chapter in therapeutic endeavors by the surgical closure of a patent ductus arteriosus has naturally led us to the belief that nearby abnormalities in

the aorta may be subject to some form of correction.

In March, 1938, at the time of beginning the present laboratory investigations, we were not aware of any other attempts to develop methods for the treatment of coarctation of the aorta. Within recent months there has come to publication the work of Blalock and Park,¹ as well as that of Blakemore and Lord,² relative to surgical approaches to this problem. We should like to place on record the following observations that have been made in the laboratory during the last seven years. These experiments have been less extensive than was originally planned, and have been curtailed by the exigencies of war. Nevertheless, they have progressed to a point where we believe that a method has been devised that is feasible for the treatment of coarctation of the aorta in human subjects.

THEORETICAL CONSIDERATIONS

Surgical attack for coarctation of the aorta could conceivably take four different forms. In the first place, the constricted zone might be by-passed by the establishment of a collateral channel. This general principle has been expounded by Blalock and Park,¹ who divided the upper thoracic aorta of dogs and closed the two ends separately. The left subclavian artery was then severed at the base of the neck, and its proximal end was turned downward so that it could be sewed into the aorta below the artificially produced obstruction. This provided a by-pass that permitted blood to flow directly from the upper aortic segment into the lower one. This method, however, has definite limitations because the shunt probably cannot transmit as much blood as the thoracic aorta normally carries. On the other hand, it is quite possible that in human subjects such a by-pass would be all that is required for alleviation of any hypertension. Probably the greatest drawback to the procedure would be its obvious destruction of existing

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collateral pathways that are known to come from branches of this subclavian artery in human beings with coarctation of the aorta

In the second place, the constricted portion of the aorta might be excised and the resulting gap bridged by the implantation of a segment of vein, utilizing the technic of Blakemore and Lord.² These authors have shown that in the dog it is feasible to replace a segment of aorta in this way. In human beings, however, it would be exceedingly difficult to obtain a segment of vein large enough for the graft. It is possible that a portion of the inferior vena cava of the same patient might be employed, or indeed a segment could be secured from autopsy material of another subject. A second drawback to the nonsuture method would be the narrowness of the aortic lumen that is necessarily imposed by the use of *vitalium* cuffs. This would be a particularly deterrent factor in young persons because the lumen of the vessel (at the metal cuffs) would be kept from increasing in diameter as the patient grew into adult life.

In the third place it is conceivable that a constricted portion of the aorta could be excised and the resulting gap bridged by implanting into it, with end-to-end suture, a segment of a vessel that had been preserved from autopsy on another subject. The practicality of such a transplant to the aorta was shown by Carrel.³ Additional promising results along this line have likewise been obtained by us in dogs, these we hope to report at a future date.

Lastly, a direct attack could be made on the lesion by cutting out the constricted segment, freeing the aortic arch and thoracic aorta and bringing the remaining ends together by primary end-to-end suture. Toward this type of therapy most of our experimental work has been directed.

LABORATORY PROCEDURE AND OPERATIVE RESULTS

Mongrel dogs with a wide range of weight, all above 18 kilograms, were employed. Operations were undertaken with intravenous Nembutal or with inhalation ether anesthesia. A tube was always placed in the trachea for administration of air under positive pressure while the left pleural cavity was open. In the earlier experiments a generous anterolateral incision in the third interspace was used, but in all subsequent operations a posterior approach (Fig 1) was found to be much more advantageous. The scapula was drawn forward, and the thorax was entered in the fourth or fifth interspace. Above this intercostal incision, one rib neck was sectioned, and below it two ribs were cut to allow sufficient exposure through the bony cage. The left lung was allowed to collapse partially while the chest was open. The distal part of the aortic arch and the superior part of the thoracic aorta were freed from the underlying vertebral column. The dissection of the aorta from its bed carried considerable risk of hemorrhage if the inter-

costal vessels were inadvertently torn off at their origins from the aorta, if this occurred, blood dissected along in the subadventitial spaces of the aorta, and such bleeding was extremely difficult to control. Conversely, if the aorta was carefully and gradually raised so that each intercostal artery could be doubly ligated and divided, the mobilization of the aorta could be completed with safety and little delay. The thoracic duct was identified and was always assiduously avoided.

The field was then ready for practice in the steps of division and reconstruction of the aorta. Two

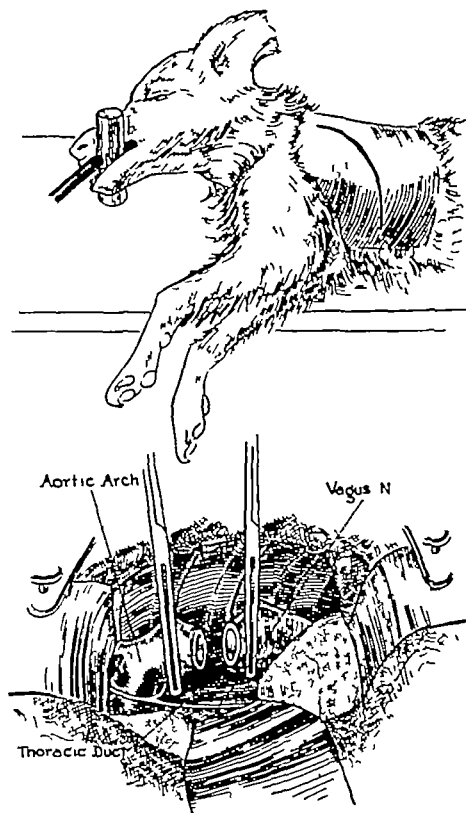


FIGURE 1 General Exposure Obtained through a Posterior Thoracic Incision

Special clamps are applied to aorta, which is then divided

clamps, several centimeters apart, were placed across the vessel to obstruct it completely, between them the aorta could be divided (Fig 1). In some cases (Table 1), a segment of aorta was cut out and discarded; there was always enough elasticity in the remaining aortic limbs to permit the cut ends to be drawn together.

The aortic clamps received a great deal of consideration and experimentation. Kelly clamps, Kocher clamps, enterostomy clamps and Bethune tourniquets were tried and discarded for one reason or another. Finally, two homemade instruments were devised from straight gastroenterostomy clamps (Fig 2), and these gave great satisfaction. The blades were sawed off and the ends fitted with a small interlocking peg, so that the blades would

not wiggle sideways when closed. The longitudinal slit in the jaws ensured against any sideslipping of the clamp on the grasped aorta. Cross markings were filed in the jaws to preclude end slipping. The

have not shown any important damage to the aortic intima or outer wall at the sites where these clamps had been used.

The total obstruction of the aorta had no im-

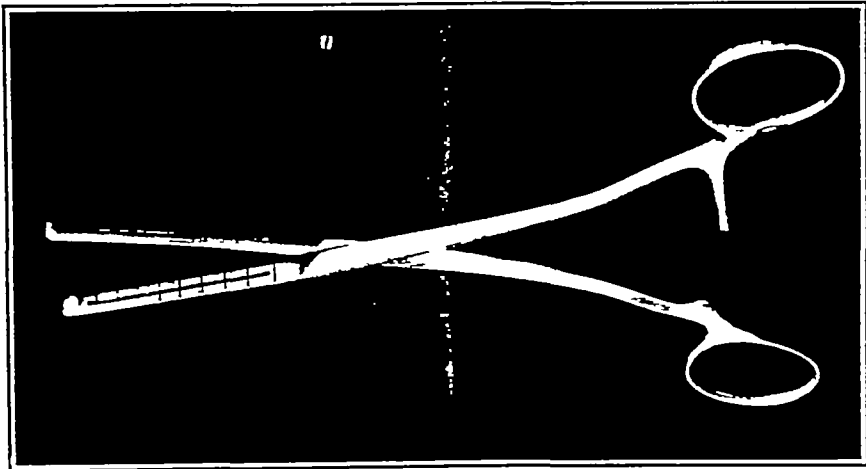


FIGURE 2 Special Clamp for Obstructing and Holding the Aorta
The longitudinal slit and the cross-markings on the jaws prevent slipping of clamp on the aorta. The peg at the end of the lower jaw interlocks with the upper jaw to keep the blades in alignment. The clamp is 18 cm. long.

jaws were springy enough so that they would adequately clutch the aorta without crushing it. These clamps gave complete hemostasis while applied to

important deleterious effects on the heart action in any of the animals. In some dogs, the heart dilated slightly. In a few, the heart rate changed to a

TABLE 1 Data on Dogs Undergoing Division and Suture of the Aorta

Dog No	DATE OF OPERATION	DATE OF DEATH	CAUSE OF DEATH	CONDITION OF SUTURE LINE	SEGMENT OF AORTA EXCISED
1	3-13-38	3-14-38	Never regained consciousness (possible anesthetic death)*	Satisfactory	None
2	3-21-44	3-22-44	Never regained consciousness (possible anesthetic death)*	Satisfactory	None
3	3-22-39	3-22-39	Cardiac failure on removal of aortic clamps	Satisfactory	None
4	4-17-44	4-17-44	Anesthesia	Satisfactory	None
5	5- 2-44	5- 7-44	Empyema	Satisfactory	None
6	5- 9-44	5-10-44	Hemorrhage	Hemorrhage from suture line (clot in lumen)	1.0 cm
7	5-19-44	1-11-45	Distemper	Satisfactory	None
8	5-26-44	5-26-44	Never regained consciousness (possible anesthetic death)*	Hemorrhage from suture line (clot in lumen)	None
9	6- 9-44	6- 9-44	Never regained consciousness (possible anesthetic death)*	Satisfactory (clot filled the lumen)	None
10	6-14-44	6-15-45	Sacrificed	Satisfactory	2.0 cm
11	6-16-44	6-19-44	Hemorrhage from chest wall	Satisfactory	None
12	6-22-44	6-26-44	Delayed hemorrhage from suture line	Late hemorrhage from suture line	None
13	1-15-45	1-27-45	Pneumonia	Satisfactory	None
14	3-16-45	6-15-45	Sacrificed	Satisfactory	1.5 cm
15	4-18-45	4-24-45	Unknown	Satisfactory	2.5 cm
16	5-31-45	5-31-45	Sacrificed (at completion of operation)	Satisfactory	None
17	5-31-45	5-31-45	Sacrificed (at completion of operation)	Satisfactory	None

*On autopsy no adequate cause for death could be found in these animals. It is possible that intracranial disturbances during the period of aortic occlusion contributed to these fatalities.

the sectioned aorta. Furthermore, they provided good handles for the assistant to steady the ends of the aorta and to pull them together so that there would be no tension on the suture line while the stitches were being placed. Post-mortem studies

minimal degree, usually slowing. In no case did a complete obstruction of the aorta prove fatal, and indeed it never produced cardiac changes of more than momentary interest.

Division of the aorta was followed by direct

end-to-end suture of the vessel, using thoroughly oiled No 00000 Deknatel silk carried on an atraumatic straight needle, 15 mm long. With great

tension on the suture line. Three general types of suturing were employed.

In a few cases the ends of the aorta were directly

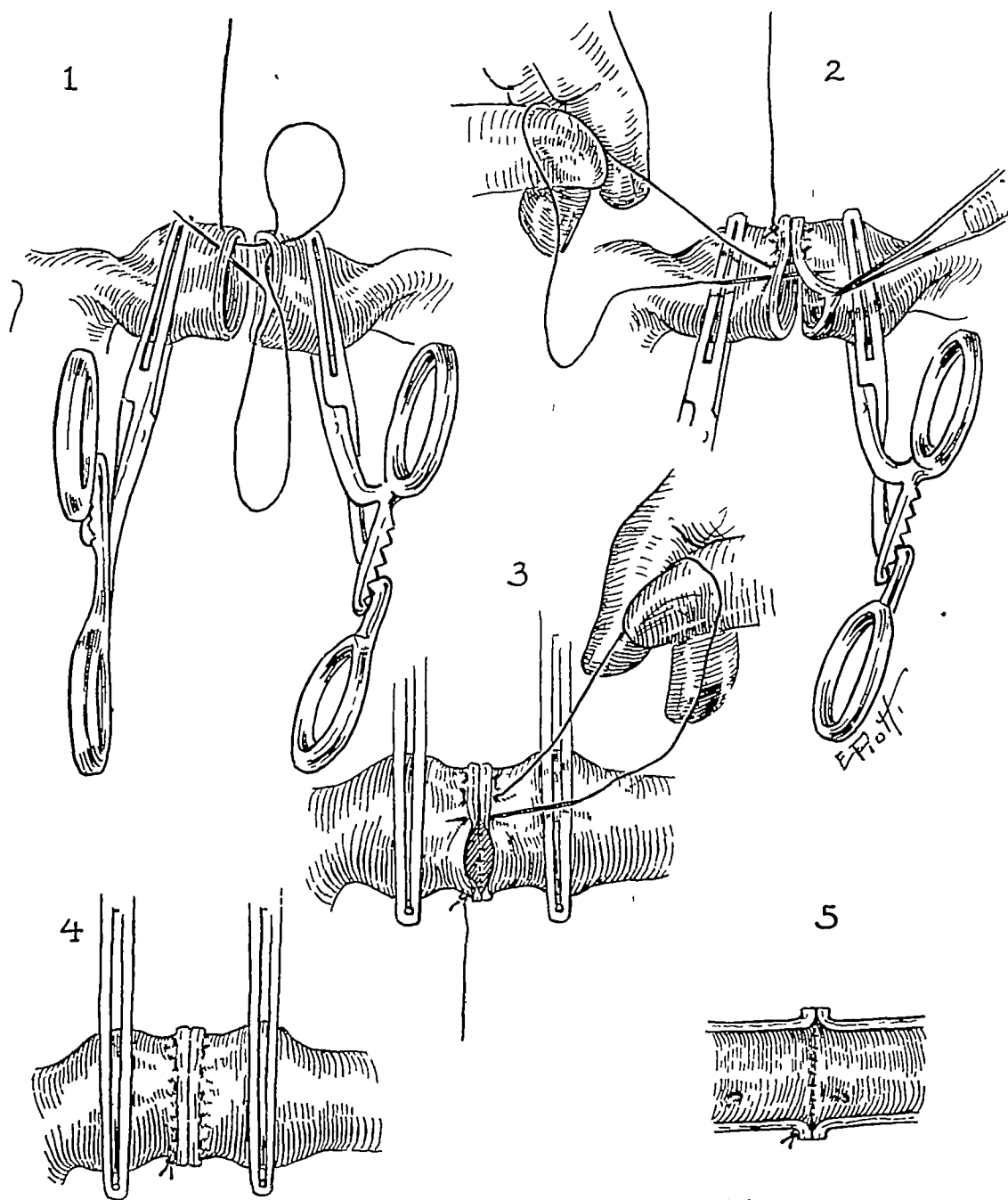


FIGURE 3 Details of the End-to-End Suture of the Divided Aorta

1 The aorta is temporarily rotated so that the back wall can be stitched first. 2 The back wall is sutured with a continuous, evert ing stitch that includes the full thickness of the aortic wall. 3 The aorta is allowed to rotate back into normal position, the back wall suture being complete, the stitch is carried around onto the front wall. 4 The anastomosis is complete, the edges of the aorta being everted. 5 A cross section shows that the intimas of the upper and lower segments are in contact with each other.

care, the first assistant held the two aortic clamps in such a way that they were pushed toward each other, hence the ends of the aorta came together and could be sewed while there was absolutely no

abutted to one another so that intima lay to intima media to media and adventitia to adventitia. To obtain this anatomic reconstruction, a continuous over-and-over suture was used to pierce the ad-

ventitia and media, but it did not include the intima, since we believed that it would be deleterious to have the silk presenting within the lumen of the aorta. In some animals this gave a satisfactory type of repair, but in others there was too much bleeding from the suture line after the clamps were removed. In spite of the theoretical and ideal considerations of attempting to keep all silk out of the aortic lumen, it was concluded that this type of repair was unreliable, and it was accordingly abandoned.

In several animals, a second form of repair was employed. The aortic ends were accurately approximated, — intima to intima, media to media and adventitia to adventitia, — with a continuous over-and-over silk stitch that included all the layers of the aortic wall. Although a firm and generous bite of the media was taken, only a millimeter or so of the intima was included in each stitch so that the amount of silk showing inside of the lumen was reduced to a bare minimum. This form of repair was distinctly superior to that described in the last paragraph, but it was by no means perfect in all cases. It, too, was occasionally followed by oozing or free bleeding from the suture line after the clamps were removed. To arrest such hemorrhage was usually time-consuming and difficult. In 3 dogs there was secondary hemorrhage at the suture line one to three days after operation, in 1 of these the loss of blood was copious enough to cause death. Surprisingly enough, the exposure of small bits of the silk stitches in the aortic lumen did not seem to present a serious drawback so far as induction of local clotting was concerned. Yet the method was discarded because it could not be counted on to give adequate hemostasis in all cases.

In the most recent animals, a third type of suture has been used, which appears to give a thoroughly reliable reconstruction. This is best described as a continuous mattress stitch, placed in such a way that the entire thickness of each aortic end is everted (Fig. 3). When each stitch is made sufficiently taut, intima is brought to intima and there is little if any silk showing on the internal surface of the anastomosis. After each stitch is taken, the silk thread is drawn up snugly and is held by a second assistant, whose sole duty is to keep it at just the right tension and to prevent the previously placed stitches from loosening. The anastomosis is begun on the posterior wall, where it is most difficult, and is carried around to and completed on the anterior surface. From time to time a little saline solution is dripped on the aorta to keep its inner and outer surfaces moist. After the continuous stitching is completed, the remaining piece of silk is tied to the original end of the silk. The aortic clamps are then removed, the lower one first. It is seldom that more than a few drops of blood exude from the suture line. If the stitching has been accurately done, there is no bleeding whatever from the anas-

tomosis line when the clamps are taken off. With increasing experience, it was found that such an anastomosis could be completed in fifteen to twenty minutes. This type of end-to-end reconstruction proved to be eminently satisfactory. It produced no constriction of the aortic tube at the site of anastomosis, indeed, the eversion of the ends tended to make the internal diameter of the aorta a little

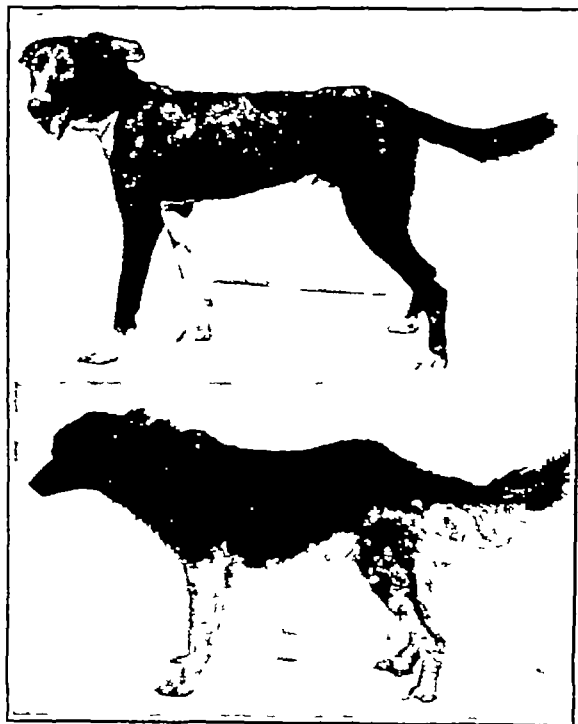


FIGURE 4. *Operative Results*

The upper photograph shows Dog 14 three months after excision of 1.5 cm. of the thoracic aorta and suture of the aorta. There is no paralysis of the hind legs. The lower one shows Dog 10 one year after excision of 2 cm. of the thoracic aorta and suture of the aorta. There is no hindquarter paralysis.

greater at this point than above and below the anastomosis (Fig. 5).

In the early part of the suture work, bleeding often occurred at the suture line after the aortic clamps were removed. In minor degrees this was not difficult to stop, but with larger leaks the area was buttressed for some minutes with a piece of skeletal muscle, fibrin foam or gauze pack. As we drew toward the completion of our operative series, we became thoroughly convinced that all these measures were poor makeshifts and were completely unnecessary if an accurate and careful repair of the third type was made.

Whenever clamps were removed from an obstructed aorta, the heart rate increased greatly and the work of the organ was obviously enormously augmented. The period of subsequent slowing of the heart usually required several minutes. This temporary rise in the pulse rate did not often seem

to be a serious affair, but 1 dog (Dog 3) died at this time — apparently of cardiac strain. It became evident, however, that the momentary embarrassment occasioned by removal of the clamps could be



FIGURE 5 Roentgenogram of a Barium-Injected Specimen of Aorta (Dog 14)

This was taken three months after division and end-to-end re-suture, with anastomosis at the level of the arrows. There is no constriction at this site.

greatly reduced if the clamps were taken off slowly in order to allow a gradual readjustment in the vascular system.

Although it had been anticipated that intraluminal clotting at the site of anastomosis might be a serious and deterrent factor to such operative procedures, this did not prove to be so. In no case was heparin or dicumarol used during or after the operation. In several animals there were clots 1 or 2 mm in size on the inner surface of the suture line, but these seemed to be of no consequence. There was a marked tendency for endothelium to cover them over in a short time. In 3 other dogs (Dogs 6, 8 and 9), all of which had either the first or the second type of anastomosis, there was a considerable degree of luminal blockage by clot at the operative site. All these dogs died within twenty-four hours after operation, and it is conceivable that clotting was promoted by the reduced blood flow, which was present in an animal dying of other causes. Except for these 3 dogs, all the animals had a satisfactory lumen of the aorta, as judged by the presence of a good pulsation in the femoral arteries and by inspection of the aortic specimen at autopsy.

A serious complication of these aortic operations appeared in the form of hindquarter paralysis in Dogs 12 and 13. Spinal-cord examinations showed diffuse degenerative changes, which had presumably

resulted from local ischemia. We were reasonably certain that such ischemia was not due to post-operative thrombosis at the site of aortic anastomosis, because these dogs had good femoral pulsations during life and had adequate lumens of the aortas when examined at autopsy. We therefore concluded that the spinal-cord damage had occurred while the aorta was obstructed by clamps during operation.

To study further the effects of temporary obstruction of the aorta, especially in relation to development of hind-limb paralysis, 20 additional dogs were operated on by opening the chest, placing a clamp on the upper thoracic aorta for a given number of minutes and then releasing the aorta. The chests were closed, and the dogs were observed for periods varying from a week to two months. Table 2 lists all these observations; it furthermore includes all the dogs from Table 1. The table is arranged in such a way as to emphasize the time during which the aorta was kept completely obstructed; these periods varied from four and a half to sixty minutes. Some dogs with occlusion of the aorta for forty-five to fifty minutes developed no paralysis, whereas others with shorter periods of aortic obstruction showed neurologic changes. In no case did paralysis develop when the aorta was obstructed for less than ten minutes. Of considerable interest are Dogs 19, 20, 21, 13, 15, 14 and 29, during operation the entire back of each animal was packed in ice. Only 1 of these developed paralysis. It seemed to us that the cooling of the animal, and probably reduction of its oxygen needs, had a distinct effect



FIGURE 6 Specimen from Dog 14

This was removed three months after end-to-end suture of the aorta. The arrows indicate the operative site. Healing of the aorta is excellent.

in sparing the spinal cord from damage during the temporary period of reduced blood flow.

Colson,⁴ Carrel⁵ and Blalock and Park¹ have commented on the correlation of aortic obstruction and hind-limb paralysis, and such studies have

been furthered by the experiments here recorded It is quite important, however, to point out that when aortic operations are performed in human subjects, there is little likelihood of neurologic complications from temporary aortic obstruction if there is an adequate collateral circulation, such as is uniformly found with coarctation of the aorta This belief is substantiated by the observations of Alexander and Byron,⁶ who, without deleterious neurologic effects, resected an aneurysm of the thoracic aorta in the presence of a coarctation of this vessel

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Since this manuscript was submitted for publication, two human patients have been operated on by one of us (R E G) for coarctation of the aorta The first was a six-year-old boy who underwent operation on June 28, 1945 Using a posterior thoracic approach, the area of coarctation was readily visualized The narrowed zone had a lumen only 2 or 3 mm in diameter Between

TABLE 2 Incidence of Hind-Leg Paralysis after Temporary Obstruction of the Aorta

Dog No	PERIOD OF AORTIC OBSTRUCTION min	TREATMENT OF AORTA	BACK OF ANIMAL PACKED IN ICE DURING OPERATION	PARALYSIS OF HIND LEGS
18	60	Clamped	No	*
7	50	Clamped severed and sutured	No	None
8	50	Clamped severed and sutured	No	*
10	50	Clamped severed and sutured	No	None
19	45	Clamped	Yes	None
20	45	Clamped	Yes	None
21	45	Clamped	Yes	None
22	45	Clamped	No	Present
23	45	Clamped	No	Present
24	45	Clamped	No	Present
9	40	Clamped severed and sutured	No	*
25	40	Clamped	No	*
1	35	Clamped severed and sutured	No	None
11	35	Clamped severed and sutured	No	None
5	30	Clamped severed and sutured	No	*
3	30	Clamped severed and sutured	No	*
4	30	Clamped severed and sutured	No	Present
26	30	Clamped	No	Present
27	30	Clamped	No	Present
12	27	Clamped severed and sutured	No	Present
2	25	Clamped severed and sutured	No	*
13	23	Clamped severed and sutured	Yes	Present
6	18	Clamped severed and sutured	No	†
17	18	Clamped severed and sutured	No	†
16	15	Clamped severed and sutured	No	None
15	15	Clamped severed and sutured	Yes	None
14	15	Clamped severed and sutured	Yes	None
28	15	Clamped	No	None
29	12	Clamped	Yes	None
30	10	Clamped	No	Present
31	10	Clamped	No	None
32	7	Clamped	No	None
33	6	Clamped	No	None
34	6	Clamped	No	None
35	5	Clamped	No	None
36	5	Clamped	No	None
37	4½	Clamped	No	None

*Died during operation or on next day
†Sacrificed at termination of operation

SUMMARY AND CONCLUSIONS

An attempt has been made to find a surgical procedure that is adaptable for the correction of coarctation of the aorta in human subjects Theoretically, it would be possible to excise such a constricted portion of the vessel and to reunite its upper and lower segments This principle has been tested in the laboratory by completely dividing the upper thoracic aorta, or excising a segment of it, and reconstructing the vessel by end-to-end suture The outcome of these experiments leads us to believe that it is technically feasible to remove a narrowed portion of the aorta in man and to re-establish its continuity by careful and accurate end-to-end anastomosis by the method herein described

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clamps, the constricted segment was excised and the remaining ends of the aorta were sewed together Through all this the child was in a satisfactory condition As soon, however, as the clamps were removed from the aorta and the enormous vascular bed was opened up, the heart suddenly went into uncontrollable dilatation and the child died This catastrophe again emphasizes the point that the aortic clamps must be removed slowly The second patient was a twelve-year-old girl for whom surgical therapy was undertaken because of marked hypertension The systolic pressure was frequently recorded at 215 and at no examination was it below 190 No pulsations could be felt in the groins or legs, and no blood-pressure readings could be obtained in the legs Operation was performed on July 6 1945 The aorta appeared to be completely blocked about 1 cm beyond the origin of the left subclavian artery The aorta was doubly clamped, and the constricted area was excised (Examination of the interior of this specimen showed no opening between its two ends) The aorta was repaired by direct end-to-end anastomosis The clamps were gradually released, a full ten minutes being taken before opening them fully There were no deleterious effects on the heart The procedure was tolerated exceedingly well, the wound healed per primam The patient was discharged from the hospital in a satisfactory condition on the nineteenth postoperative day The systolic pressure in the arms had dropped to 140 Femoral pulsations could be readily felt, and the systolic pressure in the legs was 145

THE NEED OF FACILITIES FOR THE CARE OF FEEBLE-MINDED INFANTS AND YOUNG CHILDREN

ISOBEL V DUGUID*

BOSTON

THE protective care of mentally defective infants and young children in Massachusetts is an acutely serious problem for their parents. Some are advised, or decide independently, not to take home from the hospital the infant recognized at birth to be grossly defective. Others are slower to realize the meaning of retarded development, and only when faced with increasing difficulties in the care and management of the defective child in the household group with normal children do they come to the decision that separation is desirable. Such a decision is sometimes deferred until the behavior problem and the effect on the other children, as well as on the parents, have become a hazard to the well-being of the family group. Physicians and parents frequently turn to the medical social worker for advice, in the hope that she can suggest and arrange suitable placement.

It has been known that state custodial care of these children has been insufficient to provide for more than a small number of those needing such care. There are approximately 4000 feeble-minded persons of all ages on the waiting lists of state schools for the feeble-minded. The State Infirmary at Tewksbury, an institution under the Department of Public Welfare, has accepted temporary care of some of these infants, although they are suitable charges of the Department of Mental Health. About 50 such infants are now cared for at the infirmary, and there is a waiting list for admission. Private resources within the Commonwealth are negligible (30 beds). In a study made in 1941, only 51 children under five years of age were found to be in the care of state institutions for the feeble-minded†. It seems obvious that rarely can prompt institutional admission be assured, even in the most urgent cases. Hence, it is not surprising that the social worker consulted after the knowledge of the problem has come to the parents, and often after the doctor has unequivocally advised institutional care, or consulted later in the childhood of the defective, when the burden of care has attained unbearable proportions, finds herself unable to offer a satisfactory solution in placement outside the home.

* * *

Recently, the members of a committee‡ sponsored by the New England District of the American

Association of Medical Social Workers have brought together evidence from their experience in the care of these infants and young children as the parents have sought their help. To focus the problem, it was decided to account for all mentally defective children under six years of age known to these workers between January 1, 1943, and June 30, 1944. There were 189 such children, of whom 61 were under one year, and 99 under two years of age. There were 113 boys and 76 girls.

The reports from medical social workers who were asked to help in caring for these children were supplied by the following agencies and hospitals (in Boston unless otherwise stated)

State departments	56
Public Welfare	40
Public Health	10
Education (Division of the Blind)	6
Social service departments of hospitals	133
Children's Hospital	75
Massachusetts General Hospital	23
Boston Dispensary	7
Massachusetts Eye and Ear Infirmary	6
Boston City Hospital	4
Cambridge Hospital, Cambridge	3
Salem Hospital, Salem	3
St. Luke's Hospital, New Bedford	3
New England Hospital for Women and Children	2
Springfield Hospital, Springfield	2
Quincy Hospital, Quincy	2
Beth Israel Hospital	1
Boston Lying-in Hospital	1
Memorial Hospital, Worcester	1

189

The fact that the parents of these 189 children were referred to social-service departments for advice is evidence that in each case problems were presented that the parents were unable to meet without counsel or assistance. Actually in a large majority of the cases the complications were extremely serious. All the children were feeble-minded. Nine were classified as idiots and 26 as mongols, 27 were hydrocephalic and 3 microcephalic, and many had additional neurologic or physical defects. In 60 cases the defective was the only child, in 99 cases there were one to three other children, in 26 cases there were more than three other children, and in 4 cases information regarding the number of children was lacking. Social situations within the families supplied further complications. In at least 28 cases the fathers were known to be in the armed services, in 17 the parents were divorced, in 12 the children were illegitimate, in 5 the father was dead, in 2 the mother was dead, in 2 the father was in prison, in 1 the mother was in a reformatory,

Department of Public Welfare, Ida M. Cannon, Massachusetts General Hospital, Edith Canterbury, Boston Dispensary, Catherine Gaffey, New England Hospital for Women and Children, Janet Gorton, Massachusetts Department of Education, Division of the Blind, Marion Hall, Children's Hospital, Mabel Houghton, Boston City Hospital, Eleanor Rogers, Robert Breck, Brigham Hospital, and Elizabeth Wheeler, Massachusetts General Hospital.

*Social worker, Baker Memorial Massachusetts General Hospital.

†Feeble-Minded Children as Massachusetts Problem. 63 pp. Boston Massachusetts Child Council, 1941.

‡The members of this committee are as follows: Isobel V. Duguid, chairman, Massachusetts General Hospital; Flora Burton, Massachusetts

and in 1 she was in a state school for the feeble-minded

In 80 cases placement was arranged, but of the 54 children placed in state institutions 39 were at the Tewksbury State Hospital and Infirmary, which is primarily responsible for the care of the chronic indigent sick, not the feeble-minded. Only 4 were admitted to state schools for the feeble-minded — 3 at the Wrentham school and 1 at Belchertown. Many of the other placements were either temporary or unsatisfactory, and replacement was advised in 15 cases.

As of June 30, 1944, the terminal date of the study, only 28 children had placement that could be considered permanent. Thirty-three children had died. Of the 128 others, institutional care had been recommended for all but 21, and in 54 cases it was considered to be urgent, in at least 75 cases of this group application had been made at one or more state institutions.

Among the children for whom institutional care could not be secured, characteristic problems were the following:

An only child, aged five at the close of the study, is boarded in a foster home by the mother, a widow, at \$20 a week. The mother has been the sole support of the child since the father's death three years previously. She is a cashier in a restaurant, earning \$25 a week, and works overtime to increase her income. The child is on a waiting list for a state school for the feeble-minded.

A boy, aged 4, at home at the close of the study, is one of seven children under fifteen years of age, one of whom, aged nine, is also feeble-minded. The four-year-old child, an idiot, is utterly helpless. Both children are a great strain on the mother and should be separated from the normal children.

A two-year-old girl, the eleventh child in the family, is a mongolian idiot. Her care involves neglect of the other children.

A four-year-old boy of extremely low-grade mentality is a serious behavior problem, since he is irresponsible and abusive of two younger normal children and needing constant watching by the mother.

A three-year-old feeble-minded boy, whose father is serving in the Marine Corps, is the middle one of three children. He is a serious burden to his mother, since he cannot stand, talk or feed himself nor can he control his bowels or bladder.

Such are the problems of parents and, in some cases, of lone mothers of the defective children of the Commonwealth

* * *

A realistic approach to the problem high lighted by this limited report brings sharply before one the need of substantially increasing the present resources, in terms of additional state institutions for custodial care, which maintain standards offering security both to the children placed therein and to their parents.

This provision for care might well, from an economic, as well as a social, humanitarian point of view include expansion of the present instructive and supervisory service already instituted by the Massachusetts Department of Mental Health for aid to parents in the management and care of defective children in their homes.

In this connection, the medical social workers believe that substantial help in meeting these admitted needs regarding care can probably be derived from earlier and more deliberate consideration of individual needs. The anxious and often seriously troubled parent may become more deeply disturbed by insistence that the infant should not be cared for at home, especially when it proves impossible to find a placement immediately. Experience has shown that in certain cases the defective child, far from being a monstrous object, can remain within the home at least for a time without disruption of the family, and even with greater ease of mind for the parents than if separation were effected from birth. It has been learned by the medical social worker that the mother who has been told not to see her newborn, defective baby visualizes something much worse than is really the case. Careful study and individualization in many cases, with the assistance of the social worker, would result in a more selective use of the limited resources, and in some cases might give greater help to parents in what is so often one of the greatest human problems.

CLINICAL NOTE

THE POSSIBLE INTER-RELATION OF
PSORIASIS AND *STREPTOCOCCUS*
FAECALIS

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MUCH has been learned about psoriasis, but none of the numerous theories have been substantiated by evidence that warrants a definite conclusion concerning its etiology.

Of particular interest is the fact that some cases have responded temporarily to a diet low in proteins, others to one low in carbohydrates, and still others to a low-fat intake. In many cases, however, if the patient continued on such a diet for any length of time, the improvement ceased. A change to another type of diet frequently resulted in further improvement.

It is noteworthy that there is a strong family history of psoriasis in a large group of psoriatic patients. This is also true of allergic diseases. Furthermore, Madden's¹ histologic studies of uninvolved skin of patients with psoriasis suggest a skin deviating from the normal in such cases. Both the above findings lead one to believe that psoriatic subjects may be born with a congenitally susceptible skin, which may become sensitized to the products of one or more organisms in the lower bowel.

The finding of a low redundant colon by barium enema in a small group of psoriatic patients studied, although not conclusive, suggests the stagnation and piling up of certain organisms in the lower bowel. Further studies in a larger series are necessary. Although no definite history of constipation was obtained, the following is a characteristic answer: "Shortly after a bowel movement, I feel that I could move my bowels again."

While investigating the presence of bacterial allergy in dermatitis herpetiformis, it was noted in some of the psoriatic patients used as controls that the intradermal injection of an autogenous stool vaccine brought on an aggravation of the psoriasis and a psoriatic lesion at the point of injection. The latter was thought to be Koebner's phenomenon,[†] but the exacerbation of a pre-existing psoriasis could not be so explained. By a process of elimination it was discovered that *Streptococcus faecalis* was the only organism in the stool that caused such reactions in psoriasis. Although this organism was almost always found in the stools of normal white persons, it was believed that the psoriatic lesions were possibly produced by a dilated colon favoring stagnation and a piling up of *Str faecalis* in those

born with a congenitally susceptible skin that had become sensitized to the products of this organism.

In a series of 15 cases, the intradermal administration of *Str faecalis* vaccine in proper dosage sometimes resulted in marked to moderate improvement, when too large a dose was administered, the patient was made definitely worse. In several cases a psoriatic lesion appeared at the site of injection following the undesirably large local reaction caused by a big dose. In 2 cases, swelling and pain of the phalangeal joints was associated with such doses. In 1 case, control injections of sterile water, saline solution and typhoid vaccine failed to cause such reaction.

It is my belief that there are strains of *Str faecalis* of different virulence, and that the most successful treatment with vaccine occurs when it is made from one of the less virulent strains, so that the patient can be desensitized without an untoward reaction. This belief is based on the fact that in the same subject the reaction varied with the amount and with vaccines prepared from various strains obtained from the stools. This method of treatment is not advised until further knowledge of strain and dosage has been obtained.

Another interesting point is that King² has reported that in the bacteriologic examination of consecutive stools of 14 full-blooded Negroes in an Army camp, no *Str faecalis* was found, whereas it was encountered in the stool of a mulatto. This finding appears to coincide with the fact that most Negroes do not suffer from psoriasis.

The above observations strongly suggest that the presence of a redundant colon results in an accumulation of *Str faecalis* in the bowel and that the development of sensitivity to this organism causes psoriatic lesions in a congenitally susceptible skin.

Externally applied therapeutic factors, such as ultraviolet light, ointments and the like, presumably decrease the sensitivity of the skin to the products of *Str faecalis*, at least temporarily. The remissions so characteristic of psoriasis may be explained on the basis of improved intestinal function, due in turn to seasonal changes in diet, outdoor exercise and so forth, or to unknown factors that at times so mysteriously influence the severity of other diseases of allergy, such as hay fever, asthma and angioneurotic edema.

The occasional case that is benefited by repeated transfusions of whole blood may be explained on the basis of the introduction of antibodies for *Str faecalis*.

SUMMARY

On the basis of the two following observations it seems likely that *Streptococcus faecalis* has some causal relation to psoriasis: marked sensitivity to intradermal injections of minute amounts of an autogenous vaccine made from a certain strain of

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†This term simply signifies susceptibility to psoriasis in skin areas previously traumatized.

Sir faecalis in patients with psoriasis was demonstrated, both by a local reaction to the point of producing a psoriatic lesion and by an aggravation of the pre-existing psoriasis, and in the bacteriologic examination of the stools of full-blooded Negroes, most of whom do not suffer from psoriasis, *Sir faecalis* was not found

Intradermal injections with autogenous vaccines of *Sir faecalis* in proper doses for the given case, caused improvement of psoriasis, whereas a slightly

larger dose brought on an aggravation of the symptoms. Such treatment, however, is not advised until further studies have been made and the beneficial effects from proper doses have been evaluated

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MEDICAL PROGRESS

PROCTOLOGY

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THE diagnosis and treatment of most diseases of the anus, rectum and colon have become fairly standardized over a period of years. Good therapeutic results can be obtained by careful attention to detail in history taking, examination, operative procedures and aftercare. A diagnosis can often be made on the history alone, although many serious mistakes have also occurred because of reliance on the history to the exclusion of a thorough examination by index finger, anoscope, sigmoidoscope and x-ray.

The cardinal symptoms of bleeding, pain, swelling, itching and disturbance of the normal bowel habits of the patient in question constitute the basis for a careful questioning, which will usually strongly suggest the diagnosis, easily confirmed in most cases by the standard methods of examination.

Refinements in technic, measures for the relief of pain, variations in the method of treatment and a few really new and promising suggestions are to be found in the literature of the past two years, a summary of which is presented in this review.

Rectal Bleeding

Bleeding from the bowel is perhaps the most important symptom that one is called on to explain, because its source may be relatively harmless or most serious.

Stone¹ has reported 72 cases of massive melena of obscure origin, with suggestions concerning procedure. This group consisted of 31 cases in which no cause of the hemorrhage could be found, 20 in which a possible source was located, and 21 others in which the source of bleeding was proved.

In the last group were included cases of carcinoma of the colon, carcinoma of the cardia of stomach,

cirrhosis of the liver with portal thrombosis, esophageal varices, subacute gastroenteritis, gastric ulcer, cyst and diverticulum of the duodenum, regional ileitis, Meckel's diverticulum, rupture of an artery in the rectal wall, lymphoid and myeloid leukemia and hemophilia.

In the group of 20 cases with unproved sources of hemorrhage the following conditions were also included: polyps of the colon, hypertension with arteriosclerosis, granuloma of the cecum, diverticulosis of the colon, esophageal hernia and diverticulum of the esophagus.

Stone emphasizes the importance of avoiding premature surgery, treatment for shock and hemorrhage, building up of the patient's general condition and careful search for the source of the bleeding as soon as it is safe to do so. When the source is definite, operation is indicated. Some cases never bled again, several after long intervals, and others at frequent intervals.

In the discussion of Stone's paper mention was made of two other possible sources — the so-called "red stomach," encountered in cases of cholecystitis, and bleeding due to a reduction in the coagulation time of blood by large doses of aspirin.

It is worthwhile to mention the fact that a massive hemorrhage may also occasionally be due to bleeding upward from internal hemorrhoids, with accumulation of blood in the rectum and colon until its volume produces expulsion in quantity. Rarely, a fissure may bleed profusely.

ANORECTAL PAIN

Preoperative anorectal pain is usually due to fissure, abscess or external hemorrhoidal thrombosis. Less often a low cancer, a foreign body or rectal spasm may be the cause. The cure lies in operation, except in the case of rectal spasm.

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Postoperative pain is a different problem, and various suggestions concerning prevention and alleviation have been advanced

Pruitt² emphasizes gentleness in examination and manipulation, good lubrication, proper preoperative cleansing of the bowel, the use of a nonirritating enema (plain water or a soda or saline solution — *not* soap), the use of sulfonamide drugs to reduce acute inflammatory lesions and warm sitz baths as general measures designed to reduce pain. The use of drugs injected to give prolonged anesthesia of the area is advocated if judiciously applied. Pruitt mentions the various oil-soluble anesthetics, and also quinine and urea hydrochloride, Diothane, Nupercaine and alcohol. He cautions against the delay in healing that may occasionally result, with sloughing of the tissues, abscess formation and temporary incontinence. He particularly advocates 20 per cent ethyl alcohol in water, injected in the external sphincter through perianal punctures 5 or 6 mm apart all around the circumference, about 0.3 cc being used at each point. This is done before operation, under anesthesia, and it produces anesthesia of the local area for a period of a few days to two weeks. Elimination of sphincter spasm is a big factor in the relief of pain in addition to the anesthesia produced.

Smith,³ at the Mayo Clinic, points out the needlessness of anal dilatation as a preliminary to operations low in the rectum, and cites the disadvantages inherent in the procedure, namely, edema, extravasation of blood and external bleeding.

T. E. Smith⁴ reports the use, in 522 cases, of an anesthetic solution consisting of 6 per cent butyn, 1.5 per cent procaine hydrochloride and 5 per cent alcohol in a base of sweet almond oil. Injections, averaging 20 cc, were made deeply into the ischio-rectal fossa, with care to avoid pooling of the solution and with great care to maintain asepsis. Morphine was not needed postoperatively in 62 per cent of 250 cases, and in 54 per cent of 133 cases catheterization was unnecessary.

Pruitt⁵ discusses the condition known as "rectal cramp" or "rectal spasm" encountered at intervals in one's practice, usually unassociated with any demonstrable anorectal pathology but accurately described by enough patients to warrant its inclusion as a clinical entity. The pain is spasmodic, nocturnal as a rule, high in the rectum and lasts from a few minutes to half an hour. It is a gripping pain, quite severe, and comes on and disappears spontaneously. Relief may be obtained by changes in position, walking, rubbing, hot baths or warm enemas.

BLADDER DYSFUNCTION

McCrae⁶ discusses the urinary symptoms and urinary dysfunction associated with anorectal disease or following anorectal surgery.

There have been many suggestions offered to combat this frequent postoperative complication, among them the suggestion of the instillation into the bladder of 30 cc of mercurochrome while the patient is still on the operating table. Another is the ingestion of beer as soon as fluids are permitted postoperatively. Despite the employment of these measures routinely, most patients are subjected to catheterization before relief is obtained. The author suggests the following management preoperatively, the oral administration of 100 mg of Syntropan, followed postoperatively by the oral administration of 100 mg of Syntropan in combination with 15 mg of Prostigmine. The theory prompting such medication is that the Syntropan, acting directly on the sympathetic system, has some influence on the pudendal nerve, which undoubtedly contains sympathetic fibers or some communication to the sympathetic nerve in the establishment of a reflex arc, or that there is a direct communication, which is known to occur frequently between the inferior hemorrhoidal nerve and the pudendal nerve. The Syntropan exerts a sedative influence on the sympathetic nerves, whereas the Prostigmine increases the tonus of the detrusor muscle through the parasympathetic fibers, with the usual result of normal urination. This type of management has not been successful in every case, and no such claim has been made. One reason for failure, he believes, has been timidity in the administration of sufficiently large doses of Syntropan to establish a therapeutic effect. As experience grows, he believes that failures will be fewer in number. Much of the therapeutic action of these two synthetic drugs is pure conjecture. In their clinical use, however, the many remarkable results attained have suggested other possibilities in the management of certain types of "cord bladders." Plans have been laid to do considerable animal research on the action of these drugs in the presence of bladder dysfunction of neurogenic origin. Retention of urine following proctosigmoidectomy is of common occurrence, the retention being due to atony of the detrusor muscle resulting from trauma or severance of the parasympathetic nerve fibers. The best management of this type of retention is attained with the use of tidal drainage, which passively exercises the detrusor muscle, bathes the vesical mucosa continuously with bactericidal solutions, thus combating infection, completely eliminates residual urine and prevents renal back pressure. Following the use of tidal drainage, active therapeutic measures are essential. Parasympathetic stimulation of the detrusor muscle on the one hand and its sympathetic sedation on the other tend to produce normal urination. Acute urinary retention following anal surgery may also be successfully combated by the oral administration of Syntropan and Prostigmine in combination.

Pruritus Ani

Pruritus ani is one of the most frequent of all the anal ailments, and it certainly is the most difficult to treat satisfactorily. Attempts to establish any of the other common pathologic conditions in this area as etiologic factors in the itching have been notoriously unsuccessful. Treatment has been largely symptomatic consisting of ointments, washes, the injection of local anesthetic agents (usually in an oil medium to produce prolonged effect), alcohol injections and x-ray therapy.

Boyd and Bellows⁷ report therapeutic results obtained by means of an absorption-base ointment in 50 patients suffering from anorectal diseases. The purpose prompting this paper was to direct attention to a promising pharmacologic principle—the enhancement of drug action by the medium in which it acts. Although this fact is well known and widely applied by dermatologists, it does not seem to have engaged the attention of other physicians. For a long time dermatologists studied the penetrability and absorptivity of the skin, but progress was slow and sporadic so long as the basic materials for achieving these objectives consisted of a few fats and oils, in addition, the knowledge of surface chemistry was rudimentary. The irritation produced by many potentially useful agents precluded their application. Diseases of the anorectal region permit observations of the skin and mucous membrane, and a preparation has been formulated on the basis of the principle stated above.

The ointment in question consists of lanolin and cholesterol, with 2 per cent of cetyl alcohol and a wetting agent. As stated above, such bases characteristically improve absorption and penetration of the incorporated agents. The oil phase of the preparation consists of the oils of thyme and eucalyptus, whereas the water phase is represented by the fluid extracts of hamamelis and of krameria.

The pharmacologic action of the ingredients is universally known and requires no description. In addition to the astringent witch hazel and the tannin contained in the krameria, ephedrine was included for hemostasis. Local analgesia is secured by two common anesthetics, benzocaine and chlorbutanol. An antipruritic action is obtained by the oils previously mentioned and by camphor and menthol. Since infection may play a significant part in rectal pathology, an attempt has been made to diminish it by the inclusion of zinc oxide, titanium dioxide, chlorthymol and propyl para-hydro-benzoate. The solids are present in a highly subdivided form, they are not absorbed but are deposited on the surface as a protective screen.

The results were particularly satisfactory in the patients with pruritus ani. A fair number were relieved over a period of months. It was the author's strong impression that the results were most permanent in the group of cases considered to be due to

fungus infections. Accordingly, it appears likely that dual-purpose ointments will prove to be effective in the management of pruritus ani that is of infectious origin. The use of suitable bases to permit proper absorption of anesthetic agents and to suspend insoluble particulate antiseptics for deposit on the infected surface is desirable.

In this connection it is interesting to note that 5 per cent benzocaine usually afforded adequate analgesia in the absence of a fissure. This may be attributed to the absorption base, for without it the concentration of benzocaine required for relief is often in excess of 5 per cent, that is, in concentrations frequently causing irritation.

The relief afforded in nonfungus pruritus ani was also obvious, but observation over a long period will be necessary to determine the final outcome in resistant patients with no demonstrable etiology. The same holds true for the other subjective symptoms (burning, smarting and fullness). The inclusion, however, of many patients with chronic disease who had applied various preparations with indifferent success inclines the authors to believe that their claims of relief have considerable value.

It was difficult to evaluate the objective results except in cases of pruritus ani, where the effect on the skin could be visualized.

Hemorrhoids

Yaker⁸ strengthens the thesis that there is no reason for arguing whether surgical removal or the injection of sclerosing agents is the better form of therapy for internal hemorrhoids. He believes that there is ample reason for utilizing both methods, since good results are obtained by each. The essential thing is to recognize the fact that injection treatment should be chiefly reserved for uncomplicated and moderate internal hemorrhoids, whereas the so-called "mixed type" and the advanced cases should usually be operated on.

Whitney and Angelo⁹ list in order of importance what they believe to be the essential points in diminishing postoperative pain following hemorrhoidectomy: posterior incision of the sphincter or pecten band, the use of oil anesthesia, the placing of all sutures above the mucocutaneous line, clean-cut surgery, successful preoperative and postoperative narcosis, regional, spinal or caudal anesthesia, intelligent postoperative dressings, the prevention of complications, and intelligent management of the postoperative stool.

Inflammability of Intestinal Gases

The boyhood trick of igniting a burst of flatus with a lighted match held near the seat of the trousers at the proper moment has been brought to mind again—although probably not intentionally—by Liebermann,¹⁰ who reports a case in which an intrarectal explosion occurred during fulguration

of a polyp Hydrogen and methane are the gases responsible for this startling phenomenon, and it is recommended that after introduction of a proctoscope a stream of air be passed into the rectum and out again before the use of an electric spark

Deodorant for Colostomies

Carroll¹¹ suggests the use of enteric-coated capsules containing treated and activated carbon (90 per cent) and phenyl salicylate (10 per cent) orally two or three times a day There are no untoward effects, and the results are said to be good

Condylomas

Culp and Kaplan¹² report 200 cases of acuminate condylomas treated by podophyllin with remarkable results It appears that this drug may be considered almost a specific for the disease

Podophyllin is a powder that varies in color from light brown to greenish yellow and turns darker when subjected to heat and light It is an irritant and an active purgative A 25 per cent suspension in mineral oil has proved most efficacious in the treatment of anal warts The suspension is applied with a cotton swab to the surface of the lesions This is a painless procedure, and there is no immediate reaction In a few hours the growth becomes blanched, and in twenty-four or forty-eight hours necrotic On the second or third day it begins to slough, but the adjoining normal tissue is unaffected

No certain explanation of this more or less specific action of podophyllin is possible, but a logical assumption is that the irritating power of the drug produces spasm of the small vessels, which in turn causes ischemia, necrosis and sloughing Some dehydration also seems to occur

Speare¹³ at the Proctological Clinic of the Massachusetts General Hospital, has also been using this form of treatment with success

Imperforate Anus

Wilkinson¹⁴ mentions the difficulty in determining the precise method of treatment in cases of imperforate anus in babies because of difficulty in knowing just how far above the anal skin the end of the bowel lies A low rectum, with visible bluish bulging of the retained meconium, demands only a simple incision, whereas a higher-lying bowel necessitates much more of an operation He mentions the method suggested by Wangenstein and Rice¹⁵ of x-raying the infant suspended by its feet, to allow the rectal gas to rise to the blind end of the bowel, where it can be detected in relation to a metal marker placed on the perineum Ladd and Gross¹⁶ point out, however, that gas in the bowel often does not develop to a degree that makes this method of value until fifteen to twenty hours after birth

Foreign Bodies and Injuries

Yet another bit of evidence, if it is needed, of the toughness of the British is a report by Alkako-yunlu¹⁷ of the passage by rectum of a Kocher artery forceps left in the abdomen fourteen months previously in the course of a gynecological operation The patient began to have some vague symptoms six months prior to expulsion of the clamp, but the actual delivery was attended by no complications

Reports continue to appear from time to time, as they have over the years, of misguided persons who insert various foreign bodies in the rectum either to induce defecation or for some less wholesome reason The latest object in our experience was an olive bottle, intended to stimulate an evacuation of the bowels

Not long ago, one of us (E P H) operated on a boy who had impaled himself accidentally on one of the vertical wooden rods in the back of a chair of the Windsor type that had no curved top piece on it, being in process of repair This stick, 12 mm in diameter, was driven through the sphincter just at the left of, and parallel to, the rectum for a distance of about 15 cm until its tip was easily palpable under the skin of the left groin It broke off flush with the anal skin Catheterization revealed no blood in the urine, and laparotomy showed no intraperitoneal injury but a huge hematoma that dissected across the entire pelvis, raising up the peritoneum over the bladder half way to the umbilicus, presumably due to injury of the left deep epigastric vessels The midline wound was sutured without drainage, a small incision made in the left groin over the end of the stick, which proved to be just beneath the internal oblique muscle, and the stick was pulled out in two pieces from above Convalescence was marked by some fever, controlled by penicillin, and profuse drainage from above and below Several months later, with the perianal wound still draining slightly, an exploration from below brought forth another small piece of wood, which it is hoped will prove to be the last

Bendit,¹⁸ in reporting a case of injury to the rectum following an enema, cites Gabriel and Bacon as authorities for the statement that such injuries are more frequent than is generally realized The relative lack of sensation above the mucocutaneous line makes it possible to perforate the bowel above this point without much pain This particular patient, a man of forty-nine, in a hospital for treatment for hemorrhage from an ulcer, developed abdominal pain five days after an enema, and a perforation was found just inside the anus He recovered in seven weeks, after some perianal infection and foul discharge Sulfathiazole and gas-bacillus antitoxin were used

War wounds of the abdomen, buttocks and rectum itself have been fairly numerous, and colostomies have been done freely in these cases in Army and

Navv hospitals because of a conviction that this measure is the surest and safest way to reduce infection and to prepare the patient for later reconstructive surgery. In a visit to one of these hospitals we have seen a large group of patients whose colostomies seemed to be causing them no concern, if one can judge by appearances.

Prolapse

Skinner and Duncan¹⁹ suggest still another surgical procedure for the treatment of complete rectal prolapse. Many types of operations have been utilized with varying success in this condition, which is primarily a herniation of the cul-de-sac of Douglas. Operative procedures now in use are based on one or more of three principles: narrowing of the anus and rectum, suspension and fixation of the rectum, and resection of the prolapsed bowel.

These authors report 3 cases treated by an operation which is carried out in the following manner. The patient is hospitalized for three or four days for cleansing of the bowel, being placed on a low-residue diet. Under spinal anesthesia, in the Trendelenburg position, the abdomen is opened through a low rectus incision and the sigmoid is pulled taut. The peritoneum is then incised on each side of the mesosigmoid and is reflected laterally to expose the ureters, and the rectum is then freed from the hollow of the sacrum down to the coccyx by finger dissection. Care is taken not to injure the hemorrhoidal vessels. With the rectum pulled taut the reflected flaps of peritoneum are then sutured around the bowel, converting the previously deep cul-de-sac into a high-level pelvic floor. A temporary loop colostomy is then performed, using a glass rod. The patient remains in the hospital two weeks, and the colostomy is later closed. The authors acknowledge priority in this procedure, however, to Pemberton and Stalker,²⁰ who reported a similar operation in 1939.

Fistula

No recent article on the subject of anal fistula seems to add anything to the accepted principles of treatment of this condition. Over the years numerous attempts at primary closure of the excision wounds have been made, generally with little success. The pulling down of a cuff of intact mucosa over the internal opening after dissecting upward beneath the mucosa above it has been suggested. The best results have always come from the simple incision-and-drainage procedures, in which a few cardinal principles should be observed. Location of the internal opening is the crux of the whole situation, of course, and the main sinus tract is incised from this opening to the nearest external opening. There is no virtue in excision of sinuses as against free incision and curettage of the unhealthy granulations lining the sinus tracts. Elimination of over-

hanging wound edges, consistent with reasonable conservatism with respect to removal of vital perianal skin, and elimination of overhanging hemorrhoids adjacent to the internal opening make for a smooth convalescence and rapid healing. Good aftercare prevents bridging of the wound surfaces and consequent recurrence.

Fissure

Buxton²¹ outlines the principles in surgical treatment of anal fissure that he believes give the best results. These are as follows: excision of the fissure and sentinel pile, division of the external sphincter and postoperative mineral oil, antispasmodics, hot sitz baths, and finger insertion at intervals for two or three weeks. Most surgeons would agree with these principles, except that complete division of the sphincter, although perhaps the surest procedure, is not necessary in most cases. A division of the scar tissue superficial to the sphincter, together with a few of the superficial fibers of the muscle itself, is usually quite adequate.

Pilonidal Cysts and Sinuses

The requirement of the armed forces that soldiers and sailors shall be so treated as to ensure a minimum loss of time from active duty, as well as the high incidence of pilonidal disease, has brought this subject to the forefront of the problems of Army and Navy hospitals. The old argument of open operation versus primary closure has been revived everywhere.

Peterson and Ames²² describe an operation that is a compromise, and mention a few points of interest in connection with pilonidal disease. They state that the incidence of pilonidal sinus is three times higher in males than in females of the age group of greatest usefulness for military service. It is rare in the Negro and American Indian and has not been described in the Mongolian race. These structures are best defined as epithelial-lined sinuses of congenital origin occurring over the sacrococcygeal region, superficial to the bone and in or adjacent to the midline. There are three theories of origin: invagination of the surface epithelium, remnants of the obliterated neural canal, and an analogue of Preen's glands in birds. The general trends in treatment are based on complete removal or eradication of the sinus and tracts and on preoperative care and treatment of the infection. None of the operations in common use, however, satisfactorily prevent recurrences or long hospitalization in the majority of cases. The nature of the origin of the sinus provided a clue to a simple and certain method of treatment. The operation can be carried out without a long preoperative stay on the sick list and can be carried out aboard any ship, with only about three days lost from duty. It consists in thorough opening of the cyst and tracts, with mar-

supialization of the cyst wall to fill the defect. It can be carried out in the presence of heavy infection. Bleeding is minimal, no spread of infection occurs and healing is rapid and relatively painless.

Barker and Clark,²³ in 19 cases of chronic pilonidal infection, made an elliptical incision, undermined the lateral areas and did a primary closure with nylon mattress sutures tied over buttons, after placing 5 gm. of sulfanilamide powder in the wound and over its edges. The sutures are not tied over gauze, so that the incision can be dressed frequently for cleanliness. There was only one failure in this group, but no mention is made of length of the follow-up period. The average hospital stay was about twenty days.

Rogers²⁴ has struck a sensible note regarding the treatment of this disease in the Army and Navy. Most surgeons are agreed that excision and open packing is the best insurance against recurrence. Nevertheless, because of the long convalescence before complete healing, and because of Army insistence on hospitalization until healing is complete, many methods of primary suture have been devised, there has been some success, but often the results are based on incomplete follow-up data. Rogers says, "Why operate at all on many of these cysts and sinuses?" The disease is trivial, annoyance is usually slight, and the occasional abscess can be simply drained, often with months of complete or almost complete freedom of symptoms before another develops. This point of view, he adds, relates not to civilian but to military practice, where conservative measures have much to recommend them.

Magrath²⁵ believes that the present appellation of pilonidal or sacrococcygeal cyst or sinus is unsatisfactory and that the present statistical method of reporting end results of operative procedure is misleading. Under the present system of general inclusiveness, one series of cases may present such extraordinary end results that a surgeon may attempt the same type of operation in an entirely different type of involvement, with discouraging results. He is thus influenced in discarding a perfectly good means of treating another type of disorder. Magrath believes that an accurate appellation may serve to clarify the controversial issue between packing the extirpated area to heal from the bottom up or closing to heal by primary union, thus permitting a better estimation of operative end results.

Barnett²⁶ states that military expediency demands a method of treating pilonidal cysts that requires little postoperative care and furnishes a well healed, protective scar. He believes that the recently developed technics of excision and primary closure in selected cases, in conjunction with sulfonamide therapy, offer the best solution of this problem. The more conservative method of excision and open packing, however, is indicated in many cases not

amenable to closure, and in civilian practice, it is the procedure of choice.

Stricture

Woods and Hanlon²⁷ review the general problem of inflammatory stricture and present an analysis of 192 cases over a twenty-five-year period at the Cincinnati General Hospital. They accept the generally conceded fact that the origin of these strictures lies in the disease, lymphopathia venereum, and they mention the numerous and unsatisfactory methods of treatment.

A positive Frei test was obtained in 86 per cent of 105 cases. The microscopic picture, when observed, was always that of nonspecific inflammation.

In this series, 108 patients were dilated one or more times under anesthesia. There were 4 deaths from peritonitis and 2 from shock following this procedure. Eleven patients died as a direct result of the disease at periods up to thirteen years. In a follow-up on 77 of these cases, of which 32 were mild and 45 severe, no really good results were obtained.

Colostomy produced improvement in symptoms and general condition in 41 patients. Abdominoperineal resection was done in 23 cases, and the one-stage method was employed in 16, with good results. The authors decided, however, that the two-stage method of Lahey is preferable, since it provides a colostomy, with the bowel prepared for resection at any time thereafter if deemed necessary. Resection, by one of several methods, was carried out in 35 cases without a death.

The authors condemn dilatation under anesthesia because of its dangers, and conclude that colostomy and sulfonamides make resection of the rectum unnecessary in the majority of cases.

Megacolon

McKell²⁸ reports the cases of 3 patients, aged four, four and eleven, with congenital megacolon who were treated with Prostigmine after first having a daily bouginage of the anus for three weeks to relax the contracted sphincter. These children, who had been evacuating their colons at intervals of four to seven days, were made to have daily stools. The Prostigmine dosage was 5 mg. three times a day, 0.5 mg. of ergotamine tartrate also being given to one of the children. In one case the old bowel habits returned after discontinuance of the drug, whereas in the others a daily evacuation was still being obtained one and five weeks, respectively, after cessation of treatment. The follow-up data are, of course, too short to be of value.

Whitehouse, Bagen and Dixon²⁹ reviewed 29 cases of congenital megacolon in children in whom subtotal colectomy was performed between 1909 and 1941. All were definitely classified as having Hirschsprung's disease. They consider this to be the method

of choice when medical measures and sympathectomy have proved unsuccessful

Acute Ulcerative Colitis

Sulzberger³⁰ presents a single case of acute ulcerative colitis that was thoroughly studied. This type of case, which is seen at intervals by those who have contact with many cases of idiopathic chronic ulcerative colitis, is an extremely serious problem. A large tender spleen, swelling of a knee joint, erythema nodosum and lack of response to ileostomy or to penicillin, with death from multiple perforations of the colon, were the striking features in this case. Only after use of sulfadiazine did apparent improvement occur, but this was of short duration.

Whitby,³¹ in an article on the choice and use of sulfonamides, states that sulfaguanidine is the drug of choice in the treatment of bacillary dysentery of the Flexner type. In adults, it is advocated in dosage of 9 to 12 gm daily for three days, followed by 6 gm daily for four or five days. Succinyl sulfathiazole is said to be more active against dysentery of the Sonne type.

Regional Segmental Colitis

Barbosa, Barga, and Dixon³² carried out a statistical study of 140 cases of regional segmental colitis seen at the Mayo Clinic over a twenty-year period. The etiology is unknown. The series includes only those cases which, when first seen, had no involvement of the rectum, differing thereby from the usual case of chronic ulcerative colitis. The great majority also showed no evidence of terminal ileitis, although a few patients (18 per cent) developed it as an extension from the cecum. This group of 140 cases comprised 4 per cent of cases of ulcerative colitis of all types.

It was impossible to classify the cases anatomically because of the wide variation in location and in the extent of involvement, but in all cases in which surgical specimens were obtained, the microscopical picture was similar, corresponding to that seen in regional ileitis and in diffuse ulcerative colitis. In general, the right colon was oftener and more extensively involved than the left, in contrast with the findings in diffuse ulcerative colitis.

Symptoms varied greatly, but cramps were frequent and the stools usually contained little blood. Some patients were extremely sick, with fever and toxemia. Considerable loss of weight occurred.

The diagnosis is made almost entirely by x-ray examination, which reveals narrowing, hyper-irritability, shortening or loss of haustration in a segment of colon of a patient in whom proctoscopy shows normal mucosa in the rectum or possibly just the lower limits of the higher segment of colitis.

Of the 140 patients, 90 were treated medically, and 43 surgically, whereas 7 received no treatment. The incidence of recurrence following medical treat-

ment was higher than that following radical surgery, and the authors believe that complete removal of the diseased area is the best treatment. In this connection it is necessary to resect well beyond the area of obvious clinical involvement. Stippling of the serosa indicates disease in bowel that otherwise seems normal to inspection and palpation. Succinyl sulfathiazole preoperatively seemed to be of value in making resection safer.

Hardy,³³ in a lecture delivered before the Royal College of Physicians in London, gives his answer to some of the questions that have occurred to many others regarding the problems of colon neurosis and ulcerative colitis. His ideas (partly in summary and partly by direct quotation) are as follows:

Colon neurosis and ulcerative colitis are respectively the ultimate expression of disorder and disease as we see it in the colon, but there is no evidence whatever for regarding them as successive stages in the development of one disease process. Colon neurosis begins and ends as a neurosis, and it is quite exceptional to find evidence of inflammation in the stools or through the sigmoidoscope. Ulcerative colitis is a disease *sui generis* and develops along its own special lines. Only rarely is a previous history of colon disorder obtained. There are, however, certain resemblances between the two disorders. In both the functions of the bowel are exaggerated. Only in one are there superadded the exudative manifestations of inflammatory disease. Psychological events are prominent in the history of each, and there is a close association between emotional episodes and bowel upset, but I have not recognized any special type of individual in colon neurosis, at least not so consistently as the immature personality in which the graver disorder seems to thrive. Age-incidence may have something to do with this condition, for colon neurosis tends to fall about a decade later. Other psychosomatic disorders, such as asthma, peptic ulcer, and Graves's disease, are wont to be associated with colon neurosis but not with ulcerative colitis.

When we come to consider the mechanisms that determine the ultimate tissue reaction, we are on difficult ground. It would seem from experiments of Florey (1938) that the sacral autonomic system is the final common pathway whereby many extrinsic and intrinsic factors are translated into increased or abnormal activity, in the one case keeping within the borders of the normal pattern, and in the other uncontrolled, passing from disorder into disease with exudation, tissue necrosis and secondary invasion. That such a process can occur has been revealed in the work of Wolf and Wolff (1942) on peptic ulcer.

One can even recognize resemblances between peptic ulcer, especially duodenal ulcer, and ulcerative colitis — the ingravescent onset with dyspepsia in the one and diarrhoea in the other, the tendency for periods of quiescence to alternate with periods of activity and for these to be dependent on emotional influences, and the ultimate establishment of structural disease in both. We can recognize, too, similar milestones in the progress of each, more pronounced in the commoner and better known disease, yet discernible in the other — a period of environmental stress acting on a predisposed, or ultimately producing, a sensitive constitution, a period of intermittent exaggeration of function, a period when the abnormal function has become the conditioned and inevitable response to certain stimuli, and finally a period of irreversible structural change.

He concludes

In these lectures I have tried to illustrate the general principle that certain disorders and diseases, which, for the present, we speak of as psychosomatic have their origins not in any extraneous agency but in a perversion of normal function, and to suggest as a corollary that for inquiry to be fruitful and treatment effective the evolution of events — order, disorder, disease — must be fully appreciated.

The history of medical progress shows that advance is uneven, periods of great activity being punctuated by periods of stagnation during which ground won is consolidated. We are now at the end of a period which has been dominated by the ancillary sciences, notably radiology and biochemistry, and during which the individuality of the patient has suffered some eclipse. There is evidence now of a new sense of direction to study man not only in sickness but in health, in his home as well as in the hospital, to see at first hand those social, financial and industrial impacts which are his daily lot, to learn their influence in the initiation, aggravation and perpetuation of disease, and perchance to control them so that order shall not proceed to disorder, nor disorder to disease.

Carcinoma

Because of the large number of papers constantly appearing on the subject of carcinoma of the colon and rectum, their review is beyond the scope of this paper.

Adenoma

The importance of benign adenomas or mucous polyps as a cause of bleeding from the rectum in children is stressed by Kennedy, Dixon, and Weber,³⁴ who report 11 cases. In 6 of the 11 there were polyps in the rectum as well as higher up. For this reason the observation of polyps in the rectum should always suggest the desirability of a search by barium enemas for others beyond reach of the sigmoidoscope. The higher polyps were removed either by incision of the colon or by resection of a segment, as indicated.

Cooper and McDonald³⁵ have reviewed the literature in relation to the eccrine and apocrine sweat glands of the anal region, particularly regarding the tumors that originate in these glands. The apocrine glands, which are odoriferous, develop at maturity and can be considered as accessory sexual glands. One of the authors (McDonald), in 1941, described a neoplasm whose origin was definitely traced to an apocrine sweat gland of the vulva, and in the present article is reported what the authors believe to be the first case in the literature of a neoplasm of the anus arising from an apocrine sweat gland. A woman of forty-two, who was operated for gall stones, was found to have a small cyst just external to the anus. This was removed. It measured 1.5 cm in diameter, was covered with squamous epithelium and contained within it a papillary tumor made up of glands lined by eosinophilic cells that answered the description of those found in apocrine glands. A transition from normal to tumor cells could be observed, but there were no mitoses. The authors suggest a relation between

these tumors and intraductal papillomas of the breast, which resemble them closely and probably develop from similar glands.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31361

PRESENTATION OF CASE

A sixty-one-year-old woman was admitted to the hospital complaining of back pain.

Three weeks before admission she noted sharp nonradiating pain in about the middle portion of the thoracic spine. It became worse when she leaned over. Six days before admission the pain completely disappeared. The following day there were numbness and weakness in the lower extremities, but the patient was still able to walk. Thirty-six hours later she was unable to walk. The numbness and weakness became progressively worse. She became incontinent of urine, and enemas had to be given.

Twelve years before admission she had injured the sacrum and the lumbar region of the spine in a fall and was immobilized in a plaster cast for twelve days. She had had one miscarriage and one normal child.

Physical examination revealed a well developed and obese woman in no acute distress. The pupils were regular and equal, they reacted to accommodation but not to light. Examination of the heart and lungs was negative. The abdomen was distended. The bladder was palpated half way to the umbilicus, but she suffered no discomfort. The strength of the arms was good, and the tendon reflexes of the upper extremities were brisk and equal. The abdominal reflexes were weak, the left being less active than the right. The knee jerks were weak. There was no patellar or ankle clonus. The plantar reflexes were extensor on both sides. Sensations of pain and touch were impaired bilaterally, particularly on the right below the third thoracic segment. Vibration sense was decreased below the nipples. There was tenderness over the region of the sixth thoracic vertebra.

The temperature was 98.6°F, the pulse 85, and the respirations 20. The blood pressure was 150 systolic, 80 diastolic.

On admission the urine gave a + test for albumin and contained 10 red cells and 10 white cells per high-power field. Later specimens were negative. Examination of the blood on entry showed a red-

cell count of 4,350,000, with a hemoglobin of 80 per cent, and a white-cell count of 10,400, with 78 per cent neutrophils, 20 per cent lymphocytes and 2 per cent eosinophils. The nonprotein nitrogen was 30 mg per 100 cc, the total protein 6.6 gm, and the fasting blood sugar 102 mg. A rapid Hinton test was negative. A lumbar puncture yielded a small amount of slightly xanthochromic fluid under practically no pressure. There was no increase in pressure on jugular compression. The last portion of fluid was slightly bloody. It contained 2520 red cells, 3 polymorphonuclear cells and 4 lymphocytes per cubic millimeter. The gold-sol curve was 1455555554. The total protein was 1140 mg per 100 cc, and the sugar 38 mg.

X-ray examination showed the lung fields to be clear. The lateral portion of the left half of the diaphragm was somewhat elevated, and there was obliteration of the left costophrenic angle, without evidence of fluid or other definite pathology. The heart was slightly enlarged in the region of the left ventricle. The aorta was somewhat tortuous. Films of the dorsal spine showed some osteoporosis of all the visualized bones. All the pedicles were preserved, but there was slight decalcification of the left fifth, sixth and seventh dorsal vertebrae. The disk spaces were not remarkable.

On the first hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR WILLIAM SWEET: Perhaps this is as good a time as any to see the x-ray films.

DR MILFORD D. SCHULZ: There is some loss of contour of the posterior margins of the bodies of the fifth and six vertebrae. This segment shows a little decalcification, but certainly it is not pronounced. There is no definite evidence of bone destruction.

DR SWEET: The interpretation at the time the films were taken mentioned slight decalcification of the fifth, sixth and seventh dorsal vertebrae.

A transverse lesion of the spinal cord developing this sequence of symptoms and signs in a total duration of only three weeks is likeliest, on a statistical basis, to be due to a malignant neoplasm invading the spinal canal, but before we alight on that dismal diagnosis, we should consider a number of things that suggest other possibilities.

I might first go through the symptomatology to indicate how confident we can be that the patient had some sort of a space-taking lesion. The initial symptom of pain referred to the middle portion of the thoracic spine was presumably on the basis of irritation of one of the small branches of the intercostal nerve in that particular region and could have been due to a space-taking lesion, such as neoplasm, abscess or granuloma. The rapid development of involvement of the spinal cord, once the first symptom had occurred, suggests a neoplasm that was

*On leave of absence

malignant but does not rule out the possibility — perhaps makes it likelier — that there was frank pus or a granulomatous lesion. In cases of extradural neoplasm, following the evidence of irritation to nerve root, there is usually a period of weakness in the lower limbs before sphincter disturbance and sensory loss appear, but in this case the sensory loss and weakness appeared simultaneously, which suggests either a rapidly developing neoplasm or a granuloma. I do not believe that we can get any help from the past history. The history of injury to the lumbar spine and sacrum does not, to my mind, suggest any connection with the high thoracic lesion, and the history of one miscarriage and one normal child does not point to syphilis. We must pay more attention to the fact that the pupils reacted to accommodation but not to light. We are not told whether the pupils were small, that is, whether they corresponded to the Argyll-Robertson pupil in this respect.

DR CHARLES S KUBIK The pupils were 4 mm in diameter.

DR SWEET In other words, they were of fairly good size — not so miotic as many Argyll-Robertson pupils. The blood Hinton test was negative. We know, however, that approximately 5 to 10 per cent of the cases of parenchymatous neurosyphilis do not have positive serologic reactions in the blood but do have them in the spinal fluid. This patient apparently was such an emergency that there was not time enough to wait for serologic examination of the spinal fluid. So the facts that the pupils did not react to light and that there was no serologic examination of the fluid in which the reaction might well have been positive make me pay more attention to the likelihood of syphilis than I might otherwise do. I have never seen a case in which a rapidly developing transverse lesion of the spinal cord was due to syphilis, but I looked the subject up for my own instruction and was astounded to discover papers reporting a large number of cases in the first fifteen years of the century — one paper from England¹ and another from France² — in which syphilis was the most frequent disease to produce a rapidly developing transverse lesion in the spinal canal. The reason one does not see it so often nowadays is that the medical treatment of syphilis has made rapid strides. The x-ray films show only slight osteoporosis. If we are to pay attention to this minimal decalcification in the thoracic vertebrae then I think we should consider syphilis as rather unlikely. When syphilis invades the bone it is much likelier to produce extensive osteoblastic changes than a diffuse osteoporotic or osteolytic process. These bone changes are so slight, however, that we should not place too much weight on them and perhaps put more weight on the possibility that the patient had syphilis.

There are two reasons for paying attention to the diagnosis of epidural abscess. The symptoms were

of short duration, only three weeks, beginning with pain localized over a portion of the thoracic spine, which is typical for epidural abscess. The physical examination showed tenderness over the region of a thoracic vertebra, which is also typically seen in cases of epidural abscess. Against this possibility is the fact that there was not a decisive increase in the number of white cells in the spinal fluid. The fact that it contained 3 polymorphonuclear cells and 2500 red cells per cubic millimeter, a ratio of approximately 1 white cell to 1000 red cells, suggests that slight hemorrhage was responsible for the polymorphonuclear cells, and I do not believe that we can say that she had evidence in the spinal fluid to favor the diagnosis of epidural abscess. I do not believe, either, that we get a clue from the red cells in the spinal fluid to the type of lesion invading the spinal canal, because it is not infrequent for one to find a few red cells in the spinal fluid, particularly when there is complete block, with the result that the spinal fluid does not come out below the level of block so easily as it normally does. It is then easier for a nerve root to come against the needle point and to be slightly damaged by virtue thereof. The extremely high gold-sol figures are consistent with the high level of total protein, all of which simply indicate a severe Froin's syndrome and lend no support to the possibility that the patient had syphilitic disease. To rule out the hopeful diagnosis of epidural abscess, one might also mention the fact that there is nothing in the history to suggest a source of primary infection elsewhere in the body. The patient had a normal temperature and white-cell count and apparently was not systemically ill. I have seen cases of epidural abscess in which there was no evidence of a previous focus of infection, but they did not occur in people of this age. Hematogenous infection of the epidural space and of the bones is rare in people of this age group. Also, the type of bony lesion seen in the vertebrae does not favor the diagnosis of epidural abscess or vertebral osteomyelitis. After three weeks we might expect to see slight erosion or slight osteoporosis, but it is likely to be confined to a single vertebra rather than to involve two or three.

So it looks as though we were gradually converging on the diagnosis of a malignant neoplasm, and if we are to place any weight on erosion of three vertebral bodies, we can rule out all intramedullary and all intradural extramedullary space-taking lesions. I shall proceed to the extradural space-taking lesions.

Certainly these x-ray films are not at all characteristic of tuberculosis. There is no extensive destruction of the bone such as one usually sees in tuberculosis that is accompanied by sufficient granulomatous tissue in the spinal canal to produce spinal block. The fact that the patient has a normal x-ray film of the chest also helps one to disregard the diagnosis of tuberculosis.

The four sites in the body from which carcinoma is likeliest to metastasize to bone are the prostate, breast, thyroid gland and kidney. Some 30 per cent of metastatic carcinomas in the spine come from the prostate, and 25 per cent from the breast, ovaries or uterus, the breast being by far the most frequent of the latter. In this case, the prostate, of course, is excluded. Metastasis from cancer of the breast frequently shows osteoblastic increased bone density as well as osteoclastic decreased bone density in the vertebrae. The facts that there was no increased density and that physical examination of the breasts was normal assist us materially in ruling out this diagnosis. Carcinoma of the thyroid gland often produces metastases before the primary lesion is recognizable. The slight trace of albumin and the red cells in the urinary sediment may be a clue that the patient had a renal-cell tumor. The lungs and the gastrointestinal tract are other sites for primary tumors that metastasize to the spinal canal. Again, they may show in the spine before there is any evidence of the primary location.

As for primary vertebral tumors, osteogenic sarcoma and Ewing's tumor may virtually be ruled out. They occur by far and away more frequently in the long bones of children, so that the age of this patient and the location of the disease practically eliminate either possibility. All forms of lymphoblastoma are extremely unlikely, there were no enlarged lymph nodes, nor were there changes in the blood or fever. It is still possible, however, that a lymphoblastoma diffusely invaded the three vertebral bodies and produced this picture. Multiple myeloma should be considered, although in most other parts of the body it produces a more punched-out appearance in the bone than is seen in these vertebrae. Since it may produce diffuse vertebral rarefaction, it must be considered a definite diagnostic possibility.

Primary malignant tumors of the vertebrae are distinctly less frequent than is metastatic carcinoma, so that I shall say that the diagnosis is a metastatic carcinoma arising from either the thyroid gland, kidney, ovary or uterus or, less likely, from the lungs or the gastrointestinal tract. Even if the patient had syphilis it is likelier that the involvement of the spinal cord was due to neoplasm than to syphilitic disease.

DR. MADELAINE BROWN: I was on the visit when this patient was admitted. Dr. George C. Cotzias, the resident, made a diagnosis of syphilis, probably gumma. I believed that this diagnosis certainly was a possibility, but I thought that the lesion was probably an epidural abscess.

DR. KUBIK: On what did Dr. Cotzias base his diagnosis?

DR. BROWN: The Argyll-Robertson pupils.

DR. KUBIK: That, it seems to me, was the only finding suggestive of syphilis.

CLINICAL DIAGNOSIS

Gumma of spinal cord

DR. SWEET'S DIAGNOSIS

Epidural metastatic carcinoma of spinal canal

ANATOMICAL DIAGNOSIS

Epidural gumma of spinal cord

PATHOLOGICAL DISCUSSION

DR. KUBIK: I might say that Dr. Sweet was given the serologic findings that had been obtained up to the time of operation, that is, the report was based on a rapid Hinton test which was negative. After the operation, a regular blood Hinton test and a spinal-fluid Wassermann test were positive.

Laminectomy of the sixth to the tenth thoracic vertebrae exposed an epidural mass firmly adherent to the outer surface of the dura. Most of it was removed. It was found on microscopic examination to be a gumma. We have had only one other proved case that I can find. That patient was a thirty-three-year-old man with a paraplegia that had developed gradually over a period of five months. There was a block, as in the case today, and there were 112 cells per cubic millimeter of cerebrospinal fluid. The lesion was similar to what was found in this case. It was a sharply defined mass about 5 cm in length and 1.5 cm in width and 3 or 4 mm in thickness, it was firmly adherent to the dura but did not completely encircle it. There was cellular infiltration of the dura, but little or no reaction on the inner surface of the dura.

The symptoms in these cases are apparently due to compression by the extradural mass and not to syphilis of the spinal cord. In a case of rapidly progressive paralysis, surgical decompression is probably indicated, even if one could be sure of the diagnosis. One has to keep in mind that in a patient with syphilis or neurosyphilis an unrelated condition may be responsible for his symptoms. We have had cases of both spinal tumor and brain tumor in patients with syphilis.

Does anyone know what became of this patient?

DR. BROWN: She could move one leg for a while, but the next time that I saw her the legs were completely paralyzed. I do not know the final outcome.

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CASE 31362

PRESENTATION OF CASE

A sixty-two-year-old painter was admitted to the hospital because of chest pain, cough and loss of weight.

Fifteen months before admission the patient complained of a slight amount of pain in the left chest, with cough, and at about the same time he noted

the onset of loss of appetite. Fourteen months before admission an x-ray examination allegedly showed an area of increased density in the apex of the left lung. The symptoms remained unchanged until about six weeks before admission, when the anorexia became more pronounced and the cough and chest pain more severe. He had not worked, however, for the previous six months because of the pain. He described a severe, constant ache centering in the left anterior chest, approximately over the third rib in the midclavicular line, it frequently radiated to the midline. In addition he experienced many times a day an excruciating knifelike pain that stabbed through the left chest into the region of the back between the scapulas. Cough, which had been present for many years, had recently become painful, more frequent and productive of a small amount of thick, white sputum, which never contained blood. Three weeks before admission an x-ray film of the chest had been taken in the Out Patient Department. This showed a large area of increased density in the left upper lobe. Two weeks later, bronchoscopy was negative. During the week before admission he had had night sweats and had slept but little because of pain. For many years he had had urgency and nocturia (twice).

Ten and a half years before admission the patient had a combined abdominoperineal resection for a large, Grade II adenocarcinoma of the rectosigmoid. He was discharged well in three weeks. A few days later he was readmitted and treated over a period of six weeks for cystitis and probably pyelonephritis.

Physical examination showed a well developed man, with evidence of recent weight loss. A moderately firm, nontender, freely movable nodule, measuring about 5 cm. in diameter, was felt in the left lobe of the thyroid gland, the rest of the gland was not palpable. The heart was normal in size, rate and rhythm, the sounds were somewhat distant. Chest expansion was normal and symmetrical. Except for an occasional wheeze over the left upper chest anteriorly, the chest was negative to auscultation, but there was an area of dullness over the left upper lobe posteriorly. The abdomen was normal, except for a well functioning colostomy stoma in the left lower quadrant. The extremities were normal. There was no clubbing of the fingers or toes.

The temperature, pulse and respirations were normal. The blood pressure was 130 systolic, 85 diastolic.

Examination of the urine was negative. Examination of the blood showed a white-cell count of 5900 and a hemoglobin of 85 per cent. The prothrombin time was 21 seconds (normal, 18 to 20 seconds).

X-ray examination of the chest showed a large area of density in the left upper lobe extending into the apex (Fig. 1). The left hilus was slightly elevated, and the septum between the lobes was some-

what high in the posterior portion. The left lower lung field and the right lung appeared clear.

On the eighth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. REED HARWOOD. Before discussing the diagnosis in this case, I should like to comment on the x-ray films. The lesion at the left apex does not appear to be a solid mass or tumor; its density suggests a collapsed left upper lobe, and this is corroborated by the finding that the left hilus, the



FIGURE 1 Roentgenogram of Chest

interlobar septum and the left leaf of the diaphragm are slightly higher than normal. A large tumor in this region might be expected to produce hoarseness and a Horner's syndrome, neither of which was present. I believe, then, that the lesion in the left upper lobe is a small one that has produced obstruction to the left upper lobe bronchus.

Two diagnoses occur to me to warrant serious consideration: bronchiogenic carcinoma and pulmonary tuberculosis. A metastasis from the rectal carcinoma seems unlikely for several reasons: first, because of the long period of time since his operation; second, because of the absence of other metastatic lesions; and third, because such a lesion usually arises in the parenchyma of the lung and thus is not likely to produce bronchial obstruction. No one of these reasons alone is valid, but together they seem convincing evidence against this diagnosis.

Pulmonary tuberculosis with a constriction of the bronchus must be considered. In these exercises such a lesion has been too often overlooked. In favor of this diagnosis are the duration of the symptoms and the so-called "constitutional symptoms"—anorexia, weight loss and night sweats. There are several features against this diagnosis, however, the most significant of which is the character of the chest pain. In my experience, pain is rarely present in tuberculosis, except, of course, when there is an acute pleurisy. This patient's pain appears to have had no relation to respiration. The absence of disease in the other lung is also against tuberculosis. No mention is made of an examination of the sputum, if it was done, I assume that it was negative.

In this age group, the presence of unilateral wheeze and chest pain suggests most strongly the diagnosis of bronchiogenic carcinoma. It is not at all unusual for a patient to develop more than one type of cancer. I am a little disturbed that there is no history of hemoptysis, since this is such a frequent symptom. I believe, however, that its absence does not exclude the diagnosis. The character of the pain is a little unusual, especially the recently developed knifelike pain between the scapulas. Such a pain suggests that the tumor has invaded not only the pleura but also the adjacent bony structures, either a vertebra or a rib. In fact, close inspection of the x-ray films shows a suspicious area in the fifth rib near its vertebral articulation. Although the overlying diseased lung obscures its outlines, it seems probable that this rib was involved. Such an event would be an entirely adequate explanation of the excruciating pain that this patient experienced.

There are several types of benign tumor, especially neurofibroma, that erode ribs in this region. I believe, however, that the x-ray picture is not consistent with this diagnosis.

My final diagnosis is bronchiogenic carcinoma, with extension to the pleura and ribs.

CLINICAL DIAGNOSIS

Bronchiogenic carcinoma

DR HARWOOD'S DIAGNOSIS

Bronchiogenic carcinoma, with extension to pleura and rib

ANATOMICAL DIAGNOSIS

Epidermoid carcinoma (Grade III) of bronchus, with metastasis to regional lymph nodes

PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMAN: At operation, Dr Rodolfo Herrera found a small, indurated left upper lobe, with its apical segment firmly adherent to the chest wall at the apex of the chest cavity. An extra-pleural dissection was performed, but he thought that the tumor adherent to the chest wall was not completely removed. A pneumonectomy was then carried out.

The specimen revealed an apical, solid, spherical, gray-white, granular tumor about 7.5 cm in diameter.

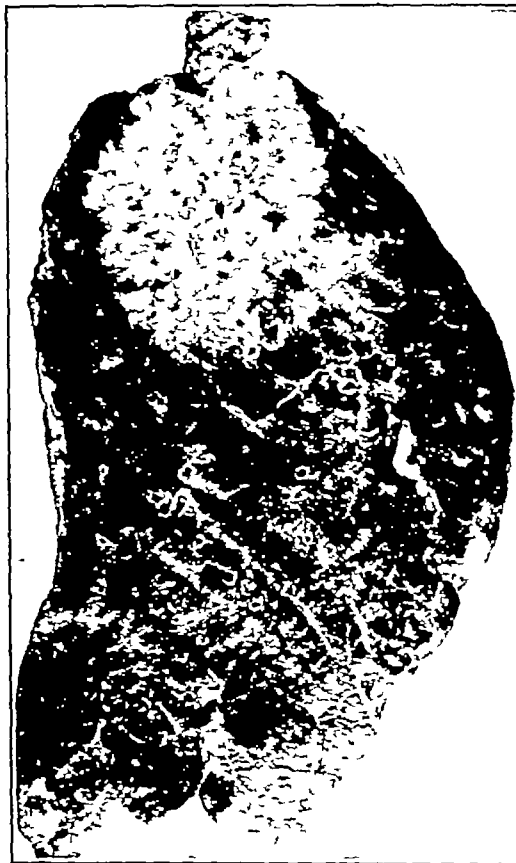


FIGURE 2 Photograph of Cross Section of Left Lung

(Fig 2) It was traversed by the posterior superior division of the upper lobe bronchus and appeared to arise from it. The lingula was not involved. There was obvious involvement of the regional lymph nodes. Microscopically, it was a rapidly growing epidermoid carcinoma.

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WAR'S END

THE war's end has come, not unexpectedly and yet with an abruptness that made it, at first, difficult to grasp, like consciousness returning to a sleeper after a bad dream or to a patient after anesthesia. The nightmare of strife through which we had been living seemed the totality of reality, without beginning and without end, relative peace seems now to be the world's normal status, and the years through which we have been passing an interlude of unreality.

So ends, like a fantasy, the greatest madness in man's history,—and may it be the last,—with all the world, save for a handful of small nations, in arms, with cities laid waste on a scale that would have

excited the envy of Joshua and with most of the servants of science and their devices turned toward the destruction of life and property. In one division alone—that of medicine—among the forces that were gathered to join the battle on the land and on the sea and in the air was modern ingenuity turned solely to the saving of life and the alleviation of suffering in friend and foe alike.

There was no alternative to our course, so far as our national obligations were concerned. A nation devoted to peace, we became committed to war, and only by making war our single purpose were we able to demonstrate that clear-cut superiority over our enemies that could end only in total victory.

We are proud that in this war the profession of medicine showed its indispensability, we are doubly proud that its military duty has always lain in the saving of life rather than in the taking of it and in the reconstruction of the human mind and body rather than in their destruction.

QUARANTINE BROUGHT UP TO DATE

OUR rules of quarantine, originally suggesting, as the word implies, a forty-day period of exclusion from the usual activities of mankind, have undergone periodic modification with increased knowledge of communicable diseases, with a decline in the severity of certain of these diseases and with improvement in the methods of control and treatment. Thus, certain of the so-called "diseases of childhood" with which we are currently acquainted have undergone natural modification in their severity within a lifetime—notably scarlet fever and measles, smallpox and diphtheria have become positively controllable, the one nearly a century and a half ago, and the other within a generation, whooping cough may be virtually controlled by the prophylactic use of vaccine, scarlet fever by immunization with toxin and by treatment with anti-toxin and the sulfonamide drugs, and measles through modification by the injection of immune globulin.

Dangerous as any disease may be in a specific case, there is no particular need for perpetuating the terror in which most of the communicable

diseases were originally held, or in continuing to accept the oppressive regulations that once encompassed them. In this relaxation of our rules of quarantine, the Massachusetts Department of Public Health has been a leading factor, modifying its regulations from time to time until now no exclusion from school is recommended for chicken pox, measles or rubella contacts and nonimmune scarlet-fever contacts are allowed to resume their academic pursuits as soon as the quarantine of the patient is removed — a minimum period of only three weeks.

Continued experience with the communicable diseases has shown that there is little occasion for any person to be afflicted with the more serious ones and has, on the whole, attested to the desirability of acquiring the others during the first decade of life. Practically everyone will agree to this principle regarding mumps, and recently reported evidence concerning the effect of maternal rubella on the fetus has shown dramatically the dangers that may be run by delaying the acquisition of this mild virus infection until adult life.

Our private schools, however, still show a distinct tendency to react with every evidence of incipient panic to the usual virus diseases with which their pupils may come in contact, although a more realistic attitude to adopt would be that of our experienced health authorities. Let the children have their exposures to chicken pox, to measles, to rubella and to mumps at a decently early age, and let them thus avoid the social and physical complications that are liable to accompany the acquisition of these infections during adolescence or in later life. It might be well, also, in the constant battle between education and communicable-disease control, to consider that education should win an occasional round.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BUSHOLD — Fred G. Bushold, M.D., of Lawrence, died June 8. He was in his sixty-fifth year.

Dr. Bushold received his degree from Tufts College Medical School in 1904.

CABOT — Hugh Cabot, M.D., of Needham, died August 14 at Ellsworth, Maine. He was in his seventy-fourth year.

Dr. Cabot received his degree from Harvard Medical School in 1898. He was formerly a member of the Mayo Clinic staff and had served as dean of the University of Michigan Medical School. As a practicing surgeon in Boston, Dr.

Cabot won prominence as a specialist in genitourinary surgery. He had been at one time a professor at Harvard Medical School and a chief surgeon at the Massachusetts General Hospital. During World War I, Dr. Cabot served with the Harvard University Unit in General Hospital 22 with the British Expeditionary Force, holding the rank of lieutenant colonel. He was a member of the American Association of Genito-Urinary Surgeons and the American Surgical Association.

His widow and three children survive.

EDSALL — David L. Edsall, M.D., of Cambridge, died August 12. He was in his seventy-seventh year.

Dr. Edsall received his degree from the University of Pennsylvania School of Medicine in 1893. In 1907 he became professor of therapeutics and pharmacology there and from 1910 to 1911 was professor of medicine. In 1912 he was made Jackson Professor of Clinical Medicine at Harvard Medical School. He became dean of the Harvard Medical School in 1918 and held this position until his retirement in 1935. In 1921 he was made dean also of the Harvard School of Public Health, likewise retiring from this post in 1935. During the early years of World War II he was chairman of the Medical Advisory Committee of the American Red Cross. He was a member of the American Academy of Arts and Sciences, the Association of American Physicians, the American Philosophical Society and the National Research Council.

His widow, three sons and six grandchildren survive.

POIRIER — Horace Poirier, M.D., of Salem, died August 14. He was in his sixty-eighth year.

Dr. Poirier received his degree from Laval University, Faculty of Medicine, Quebec, in 1902. He served as chief of obstetrics at Salem Hospital until last fall, when he resigned this position, but continued on the regular medical staff on which he had served since 1927. He was president of the Essex South District Medical Society from 1939 to 1940 and nominating counselor from 1940 to 1941.

His widow, a brother and two sisters survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JULY, 1945

DISEASES	RÉSUMÉ		
	JULY 1945	JULY 1944	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	35	23	4
Chancroid	2	1	*
Chicken pox	363	638	402
Diphtheria	13	14	9
Dog bite	1263	1041	1163
Dysentery bacillary	44	23	16
German measles	62	60	60
Gonorrhea	537	356	355
Granuloma inguinale	1	1	*
Lymphogranuloma venereum	4	3	*
Malaria	136	66	0
Measles	737	876	1159
Meningitis, meningococcal	13	27	5
Meningitis, Pfeiffer bacillus	1	1	1
Meningitis pneumococcal	3	2	4†
Meningitis staphylococcal	0	0	0†
Meningitis streptococcal	0	2	0†
Meningitis, other forms	2	1	1†
Meningitis undetermined	0	5	4†
Mumps	687	434	431
Pneumonia lobar	112	85	146
Salmonella infections	8	11	9
Scarlet fever	263	241	241
Syphilis	321	303	388
Tuberculosis pulmonary	289	213	255
Tuberculosis other forms	12	17	22
Typhoid fever	0	2	4
Undulant fever	3	3	4
Whooping cough	587	283	445

*Made reportable December 1943

†Four year average

COMMENT

Anterior poliomyelitis cases for July exceeded those for any July since 1935 and represent a number eight times the seven-year median. This does not necessarily mean that a

large outbreak is imminent. The August figure will be a better indicator. Not infrequently the July figure is not a forecast of the year's total.

Mumps showed the highest incidence in July for any year since it was made reportable in 1915.

Bacillary dysentery increased from 1 case in June to 44 in July because of the understandable difficulty of controlling this disease in institutions, especially those handling mentally defective patients, with the present labor shortage.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Beverly, 1, Boston, 9, Dedham, 1, Everett, 2, Gloucester, 2, Hardwick, 1, Holyoke, 1, Leominster, 1, Lowell, 1, Marblehead, 2, Marshfield, 1, Medford, 1, Montague, 1, Peabody, 1, Reading, 1, Salem, 4, Somerville, 1, Springfield, 2, Ware, 1, Yarmouth, 1, total, 35.

Diphtheria was reported from Boston, 2, Fairhaven, 1, Haverhill, 1, Lowell, 1, Lynn, 1, Medfield, 1, New Bedford, 2, Newburyport, 1, Quincy, 1, Revere, 1, Springfield, 1, total, 13.

Dysentery, amebic, was reported from Camp Edwards, 1, Regional Hospital, Waltham, 1, total, 2.

Dysentery, bacillary, was reported from Camp Edwards, 1, Waltham (W. E. Fernald School), 20, Worcester (State Hospital), 23, total, 44.

Malaria was reported from Bedford, 1, Boston, 1, Camp Edwards, 53, Cambridge, 1, Cushing General Hospital, 5, Chelsea, 1, Fort Devens, 43, Gloucester, 1, Haverhill, 1, Holyoke, 1, Lawrence, 2, Lynn, 1, Medford, 1, New Bedford, 1, Somerville, 2, Stoughton, 1, Waltham (Regional Hospital), 19, Worcester, 1, total, 136.

Meningitis, meningococcal, was reported from Boston, 5, Easthampton, 1, Fall River, 1, Greenfield, 1, Hull, 1, Medford, 1, Millbury, 1, North Adams, 1, Springfield, 1, Uxbridge, 1, total, 14.

Meningitis, Pfeiffer-bacillus, was reported from Canton, 1, Southbridge, 1, total, 2.

Meningitis, pneumococcal, was reported from Boston, 1, New Bedford, 1, Worcester, 1, total, 3.

Meningitis, other forms, was reported from Medford, 1, Somerville, 1, total, 2.

Salmonella infections were reported from Boston, 1, Falmouth, 1, Malden, 2, Northampton, 2, Salem, 1, Salisbury, 1, total, 8.

Septic sore throat was reported from Boston, 8, Cambridge, 1, Easton, 3, Haverhill, 1, Marion, 1, Merrimac, 2, Quincy, 1, total, 17.

Tetanus was reported from Lowell, 1, Lynn, 1, Plymouth, 1, total, 3.

Trachoma was reported from Salem, 1, total, 1.

Undulant fever was reported from Gloucester, 1, Holyoke, 1, Revere, 1, total, 3.

MISCELLANY

ANNUAL PRIZE SUBSCRIPTION

The annual prize subscription offered by the *New England Journal of Medicine* for the best undergraduate contribution to the *Tufts Medical Journal* has been awarded to Eugene G. LaForet for his paper "Medical Aspects of Submarine Warfare," which appeared in the March, 1945, issue. The paper "Myasthenia Gravis. A complete review" by Albert M. Starr and Bance M. Webber received honorable mention; it appeared in the January, 1945, issue. According to custom, these students will be given a two-year and a one-year subscription to the *Journal*, respectively.

CORRESPONDENCE

PEACETIME CONSCRIPTION

To the Editor: In the August 2 issue of the *Journal* it is stated editorially that "in view of the biologic and psychologic facts that every doctor knows, it is the duty of organized medicine and of each individual physician to throw themselves vigorously into the debate in favor of peacetime conscription." I believe that there are at least three points that merit serious meditation before one comes to any final conclusion in this matter.

Certainly there is little doubt that peacetime conscription would "improve the physical fitness of the Nation's young men" whether or not this is the best method that could be devised seems open to considerable questioning. A sizeable proportion of our physically unfit achieve this status long before they reach draft age. Will military training help these individuals more than preventive measures in infancy and in the schools? Many persons feel that late marriages among our business and professional classes, with their consequently lowered reproductive rate, are partly responsible for weaknesses in our stock. This factor would seem to be aggravated rather than helped by conscription.

Your editorial completely ignores the social and psychologic effects of peacetime military training. This method has been used extensively by many nations in the past in an effort to produce superior physical specimens, but it is questionable if they succeeded in producing superior men in other respects. For while military organizations are unequalled for training and indoctrination, their fame as truly educational institutions is not so striking.

A third point was neglected in your editorial. It was admitted that many intelligent groups were sharply divided in their opinions on this subject. Does it not seem somewhat strange that organized medicine should take such a definite stand on a question that others find debatable, without giving serious and prolonged consideration to factors other than physical fitness?

GEORGE W. COMSTOCK, M.D.

206 High Avenue
Cleveland 15

CAROTID BODY

To the Editor: The July 19 issue of the *Journal* contains an article entitled "Tumor of the Carotid Body" by Dr. Horace K. Sowles. In it he states "Physiologically it [the carotid body] is apparently of no great importance. There is little or no evidence in favor of including it among the glands of internal secretion. The facts that it is sometimes absent and that bilateral extirpation can be carried out without any subsequent symptoms suggest that its function, whatever it may be, is negligible. This being so, the only clinical interest in the carotid body is its pathology."

I should like to point out that Cornelle Heymans received the Nobel Prize in Physiology in 1938 for his investigations on the functions of the carotid body, which started in 1932. Since that time there have been a large number of articles (listed in the *Index Medicus* under the heading "Carotid Body") dealing with the physiologic importance of the carotid body, including a number of review articles in the English literature and one clinical review article (*Am J Med Sc* 208: 681-694, 1944). It is now well known by all physiologists that the carotid (and aortic) bodies are sensory receptors which are stimulated by certain chemical changes in the arterial blood. These receptors respond to low oxygen tension, decreased pH, increased carbon dioxide tension and certain drugs, such as cyanides, nicotine and so forth. When stimulated, these chemoreceptors produce a reflex increase in respiratory rate, depth and minute volume, an increase in sympathetic nervous activity (increase in pulse rate, arterial blood pressure, vasoconstrictor tone and liberation of adrenalin) and an increase in cerebral cortical activity. Although it is true that the chemoreceptors are not essential to life in a normal person, they are of great importance in those clinical emergencies in which the patient suffers from anoxia, since the main defense of the organism against anoxia resides in these chemoreceptors.

JULIUS H. COMROE, Jr.

Laboratory of Physiology
University of Pennsylvania School of Medicine
Philadelphia

RESTORATION OF LICENSE

To the Editor: At a special meeting of the Board of Registration in Medicine held July 30, the Board voted to restore the license of Dr. Herbert N. Gerardell, of East Boston, to practice medicine in the Commonwealth.

H. QUIMBY GALLUPE, M.D., Secretary
Board of Registration in Medicine

State House
Boston

BOOK REVIEWS

Immuno-Catalysis By M G Sevag, Ph D With a preface by Stuart Mudd, M D 8°, cloth, 272 pp, with 19 tables Springfield, Illinois Charles C Thomas 1945 \$4 50

That "all proteins — antigens, enzymes, hormones and so forth — are endowed with catalytic activity," is the text of this immunochemical homily. Antigenicity is considered a manifestation of catalytic (enzymatic) activity, the antigen itself corresponds to the enzyme, for which globulin "factors" serve as substrate, with antibodies as the product. The neutralizing actions of antibody on antigen are compared with the effects on enzymes of specific inhibitors structurally related to the substrate, and formed during the course of the reaction. The well documented development of this thesis occupies the first half of the monograph. The second half deals with the behavior of enzymes — in the customary, more restricted sense — as antigens, and describes the corresponding antibodies.

The whole work possesses three distinct values: a reservoir of references dealing with the relation of antigens and antibodies, a synthesis of multiplex data into a hypothesis of engaging simplicity and, finally, a catalyst that will certainly increase the velocity of immunochemical research.

Familial Susceptibility to Tuberculosis Its importance as a public health problem By Ruth R Puffer, Dr P H, Tennessee Department of Public Health 8°, cloth, 106 pp, with 9 figures and 21 tables Cambridge Harvard University Press, 1944 \$2 00

This monograph attempts to translate the factors that turn tuberculous infection into disease. Since the discovery of the causative agent of tuberculosis, scientists, clinicians and public-health workers have delved into the mysteries of resistance. At the present time, the fact is fairly clear, and practically universally accepted, that direct heredity, in the sense that the disease, like syphilis, is transmitted *in utero*, does not exist in tuberculosis. Furthermore, that certain families have a predilection for tuberculosis cannot be explained entirely by household infection. The author reviews quite thoroughly all the work done on this subject, especially that on monozygotic and dizygotic twins, and summarizes the studies on siblings, consorts and offsprings, as well as on the parents of the tuberculous. She concludes that all these studies implicate familial susceptibility as a determinant in the development of tuberculosis. She agrees, of course, that the immediate risk is greatest for susceptible persons who have unusual exposure to tubercle bacilli. Since causation of tuberculosis is a matter both of susceptibility and of exposure, with varying intensity of each, a distinct separation is difficult to obtain. Hence, she pleads for research in the discovery of the factors in the host that determine the resistance or susceptibility to the organism.

Unfortunately, Dr Puffer points only to the well known and tried form of attack against tuberculosis, namely, the search for the disease among contacts especially among members of the family. This principle has applied for the past quarter of a century. Whether or not certain biologic factors exist in certain vulnerable families is still in the realm of conjecture. Undoubtedly social and economic factors of families must also receive consideration. This monograph, however, should serve as a stimulus for further research in the causation of tuberculosis along biologic as well as bacteriologic points of view.

The Marijuana Problem in the City of New York Sociological, medical, psychological and pharmacological studies By the Mayor's Committee on Marijuana 8°, cloth, 220 pp, with 53 tables Lancaster, Pennsylvania Jacques Cattell Press, 1944 \$2 50

The New York Academy of Medicine in 1938, at the request of Mayor LaGuardia, appointed a special committee to study the marijuana problem in the City of New York. The work of the committee was divided into two major divisions:

sociologic and medical. The medical portion was subdivided into clinical, physiologic and pharmacologic.

The sociologic investigation was conducted by trained members of the New York Police Force. They found that the drug was being used extensively in Manhattan, mostly in Harlem, and that the majority of the smokers were Negroes and Latin Americans. They also found that smoking of the drug is not habit-forming in the medical sense of the word and that it does not lead to morphine, heroin or cocaine addiction. The subcommittee on sociology arrived at the conclusion that the drug is not the determining factor in the commission of major crimes, that smoking of the drug is not widespread among school children and that juvenile delinquency is not associated with the use of marijuana.

The clinical study was based on the findings in 72 subjects drawn from penal institutions, determined by a test group of five persons who had had no previous experience with marijuana. The most consistent effect observed was an increase in pulse rate. There was in general an increase in the blood sugar level and in the basal metabolic rate, but in the majority of cases the levels reached did not exceed the high normal limits. An increase in the frequency of urination was often observed, but there was no appreciable increase in the total amount of urine passed during the drug action. Hunger and an increase of appetite, particularly for sweets, were noted in the majority of the subjects, and the taking of candy, sweets and drink inhibited the effects of the drug. Nausea and vomiting occurred in a number of cases. The blood showed no changes, and the circulation rate, vital capacity and tests of kidney and liver function were not different from those of the control period. The positive results observed were not intensified by an increase in dosage, for they occurred in an equal degree after the administration of any of the effective doses used. The alteration in the functions of the organs studied apparently resulted from the effects of the drug on the central nervous system, a direct action on the organs themselves was not observed.

The psychologic tests were carried out on 54 persons — 36 marijuana users and 18 non-users. It was found that the function most severely affected was body steadiness, including hand steadiness. The ataxia is general in all directions, rather than predominate in any particular axis. The effects produced by large doses are systemically greater than those brought about by small ones. The effect of the drug runs a cycle of about eight hours, reaching a peak at the fourth hour. It affects women essentially the same as men, except that the former sometimes reach the peak and the end of the effects more quickly than the latter. The drug taken in pill or in cigarette form has a transitory adverse effect on mental functioning, and the extent of intellectual impairment is related to the amount of drug taken. Indulgence in the drug does not appear to result in mental deterioration. Comprehensive tests were made on the emotional reaction and on the effect on personality, and it was found that changes in basic personality structure did not occur but that some of the superficial aspects of behavior showed alterations. The subject experienced increased feelings of relaxation, disinhibition and self-confidence.

An extensive pharmacologic study was made of crude marijuana preparations and of cannabitol. This study led to the discovery of the active principles, the elucidation of their origin and the assembling of data concerning their chemical structure and biologic activity. The typical effects of marijuana on man are ascribed to actions on the central nervous system.

This monograph should find its place in all medical, public-health and sociologic libraries as a standard reference work on the subject.

Manual of Clinical Mycology By Norman F Conant, Ph D, Donald S Martin, M D, David T Smith, M D, Roger D Baker, M D, and Jasper L Callaway, M D. Prepared under the auspices of the Division of Medical Sciences, National Research Council 12°, cloth 348 pp, with 148 illustrations Philadelphia and London W B Saunders Company, 1944 \$3 50

The study of medical mycology has progressed slowly, due to lack of interest by physicians and in most medical schools, and has been hampered by the confusing mycologic

nomenclature found in most textbooks. Conant and his associates have avoided this error and have presented an understandable classification by simplifying the nomenclature, using only a few well recognized synonyms of the fungi. Instead of the usual introduction discussing cryptogamic botany, about which few physicians are interested, this book starts with the diseases caused by the fungi, a separate chapter covering each disease. Experts in their respective fields contribute a section for each chapter, these include a mycologist, a bacteriologist, a pathologist, an internist and a dermatologist.

Each disease is clearly defined. Its geographic distribution is illustrated by text and picture, the source of infection is noted, and the age, sex and occupation incidences are quoted. The occupational factors of thirteen diseases should be of interest to the industrial physician. The symptomatology is clearly and adequately described. The methods of laboratory examination are so well outlined that even a novice should be able to confirm the clinical diagnosis. The pathologic descriptions are clear cut and readable, the illustrations are numerous and excellent.

The reviewer's only criticism is that 208 pages are devoted to rare diseases, particularly the deep-seated infections, whereas only about 80 pages concern the frequent and widespread dermatomycoses, however, so much has been written about the latter and so little is known about the former that perhaps this is a good fault. In these days of therapeutic interest in the antibiotics, the chapter on contaminants is alone well worth the price of the book. The chapter on the immunology of the dermatomycoses, with its frequent references to trichophyton and oidiomycin, will probably be questioned by some dermatologists. The appendix contains many useful diagnostic and therapeutic formulas.

It is a book that should be in the library of every medical laboratory worker, medical student and clinician.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Tropical Medicine. By Sir Leonard Rogers, KCSI, CIE, LL.D., MD, BS, FRCP, FRCS, FRS, and Sir John W. D. Megaw, KCIE, BA, MB, DSc (hon.). Fifth edition, 8°, cloth, 518 pp., with 2 colored plates and 87 text-figures. Baltimore: Williams and Wilkins Company, 1945. \$5.75.

The text of this well known book has been revised in the light of the special needs of military medical officers serving in tropical countries. Many parts have been entirely rewritten, especially the chapters concerning malaria, the dietetic diseases, leprosy, kala-azar, trypanosomiasis and the fevers of the typhus group. The text is well printed with a good type and should serve as a standard reference work on the subject.

My Second Life. By Thomas H. Shastid, MD, LL.B., Sc.D. 8°, cloth, 1174 pp., with 130 illustrations. Ann Arbor, Michigan: George Wahr, 1944. \$10.00.

Dr. Shastid in this second book of his autobiography includes principally material not contained in the first, which was published under the title *Tramping in Failure* in 1937. The doctor writes of his childhood, his youth and his experiences in the practice of medicine in Pike County, Illinois.

The biography is written in a narrative form and is interspersed with a great many stories of local persons and conditions. He tells of his travels abroad and of his interest in medical history, fostered by his professorship at the American Medical College in St. Louis. There is an interesting story of Dr. J. M. Hewitt, in which it is claimed that he made the first roentgenogram in the Western Hemisphere in 1895, when he photographed Dr. Shastid's hand with a borrowed Crookes's tube. The picture of the hand is reproduced, but it is unfortunate that the exact day in 1895 was not recorded. This volume should prove interesting in any biographical collection.

Massage and Remedial Exercises in Medical and Surgical Conditions. By Noël M. Tidy, T.M.M.G., member of the Chartered Society of Massage and Medical Gymnastics and sister-in-charge of the Red Cross Massage Clinic, High Wycombe, England. Sixth edition, 8°, cloth, 480 pp., with 190 illustrations. Baltimore: Williams and Wilkins Company, 1944. \$6.00.

The principal alterations in this edition of a standard work have been made in the sections on fractures, which, in part, have been entirely rewritten to bring them more into line with modern methods of treatment.

Handbook of Industrial Psychology. By Dr. May Smith. 8°, cloth, 304 pp. New York: Philosophical Library, 1944. \$5.00.

This book has been written as an introduction to its subject and does not claim to be a complete treatise. In order, the author discusses fatigue in industry, industrial plant environment, job placement, time-and-motion study, temperaments of workers, especially the nervous type, maladjustment of workers and time lost in industry.

Penicillin in Warfare. A supplement to Vol. XXXII, No. 125 (July, 1944), of the *British Journal of Surgery*. 4°, paper, 115 pp., illustrated. Baltimore: Williams and Wilkins Company, 1944. \$2.50.

In this volume a number of military physicians have collaborated in discussing the use of penicillin as a therapeutic measure in wounds and infections occurring in war areas. Among the subjects discussed are fractures of the femur, gas gangrene, wounds of the chest, head and spine, clostridial infections, gonorrhea and syphilis. An interesting article discusses the prophylactic use of penicillin in the wounds of aerial warfare. A good bibliography completes the volume. This essential reference source should be available to all surgeons.

NOTICES

METROPOLITAN STATE HOSPITAL

The eleventh Postgraduate Seminar in Neurology and Psychiatry will begin Monday, October 1, at the Metropolitan State Hospital, 475 Trapelo Road, Waltham. The program consists of eighty-one two-hour lectures, demonstrations and round-table conferences in anatomy, applied physiology, pathology and roentgenology of the nervous system, clinical neurology, psychopathology and psychiatry.

The lectures will be held every Monday from October 1 to December 10, 1945, and from January 7 to April 22, 1946, in three two-hour sessions from 2:00 to 10:00 p.m. The seminar is open to all graduate physicians. Those interested are requested to register October 1 at 1:30 p.m. at the Metropolitan State Hospital.

(Notices continued on page xix)

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THE EFFECT OF CHEMOTHERAPY ON THE DURATION OF THE CARRIER STATE FOLLOWING SCARLET FEVER*

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THE utilization of chemoprophylaxis in the control of infections spread by the respiratory tract is a recent development that is gaining ever wider application. In 1939 it was shown that sulfanilamide was effective in preventing streptococcal upper respiratory infections and relapses in rheumatic fever.¹⁻³ Kuhns et al.⁴ found that sulfadiazine, when given prophylactically, diminished meningococcal carrier rates as well as the incidence of meningococcal meningitis. During the course of a scarlet-fever epidemic in a United States naval station, the routine administration of prophylactic doses of sulfadiazine to healthy contacts appeared to be effective in checking its spread.⁵

Conflicting reports have appeared concerning the efficacy of the sulfonamides in preventing complications following upper respiratory infections. Rhoads and Afremow⁶ found that sulfanilamide did not reduce the incidence of sequelae in cases of pharyngitis and tonsillitis. Kernan,⁷ on the contrary, observed that complications were decreased when patients with tonsillitis were treated with this drug. Quite recently it was observed that sulfadiazine in a solution of ethanolamines (Pickrell's solution) administered as a spray to the nose and throat reduced the frequency of bacterial infections following the common cold.⁸ Although Cecil et al.⁹ found that the sulfonamides did not alter the course of the uncomplicated "cold," there was some evidence that in certain cases secondary infections were prevented by the oral use of sulfadiazine. Bacteriologic studies revealed a constant reduction in the total number and variety of pathogens cultured from the upper respiratory tract following the administration of 3 gm. of sulfadiazine daily for four days.

The occurrence of two small outbreaks presented an opportunity to study the effect of chemoprophyl-

axis on the spread of scarlet fever. Although many workers have studied the efficacy of sulfonamides in preventing complications of scarlet fever, little thought has been given to the possibility that treatment of scarlet fever with this group of drugs may reduce the incidence of secondary cases. Among 38 hospitalized cases of scarlet fever, we have observed that 32 patients when discharged from the isolation unit still harbored the identical organism that was present on admission. It is apparent that the problem of late secondary cases is closely linked with the prolonged carrier state that may follow scarlet fever.

PURPOSE AND METHOD OF STUDY

The purpose of this study was therefore to determine whether chemotherapy reduces the duration of the carrier state in the scarlet-fever cases observed in these two epidemics. At the same time, in an attempt to prevent the possible occurrence of secondary cases among the contacts, exposed persons were given small daily doses of a sulfonamide preparation. Unfortunately, the number of contacts in both epidemics was so small that it was impractical to divide them into two groups, one to receive chemotherapy and the other to remain untreated. Nevertheless, interest was centered on the period of communicability of the treated and untreated cases.

Cases that occurred in the first outbreak were treated with sulfamerazine. The duration of the carrier state of these cases was compared with that of cases occurring in the second outbreak, all but 2 of which received no chemotherapy during the acute stage of the disease. Contacts in the first epidemic received small daily doses of sulfamerazine, whereas those in the second were treated with daily applications of Pickrell's solution as a spray.

To evaluate as accurately as possible the immunity status of persons carrying Lancefield Group A streptococci in the nose and throat, the Dick test was performed on all contacts. Serial nose and throat cultures were utilized to determine the duration of the carrier state in cases and contacts.

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In addition to the investigation of the outbreaks, further studies on the duration of the convalescent carrier state were made by serial nose and throat cultures of sporadic cases admitted to two contagious hospitals. In one of these institutions, in which chemotherapy was utilized only for severe cases, we observed 13 patients treated with sulfadiazine and 26 untreated cases. The majority of the sulfadiazine-treated patients were from six to twelve years of age and were given 0.5 gm. of the drug every four hours for seven to ten days.

In the second institution where scarlet-fever patients had been treated routinely with sulfathiazole, three groups of cases were studied. One group (12 cases) received no chemotherapy, the second (16 cases) received sulfathiazole, and the third (13 cases) received Pickrell's solution as a spray. Children above the age of six received 0.5 gm. of sulfathiazole five times daily for five to seven days. The Pickrell's solution was administered as a spray to the nose and throat four times daily for twenty-one days. The observation period varied from five to nine weeks.

BACTERIOLOGY

Nose and throat swabs were streaked on 5 per cent horse-blood agar and cultured in beef-heart infusion broth. All mediums contained 0.005 per cent para-aminobenzoic acid¹⁰. Plates were examined after eighteen to twenty-four hours incubation at 37°C and typical beta-hemolytic colonies were fished to beef-heart infusion broth. If hemolytic streptococci were not isolated from the original plate, the broth culture of the swab was appropriately diluted and streaked on blood agar. All Lancefield¹¹ Group A hemolytic streptococci were typed by the slide agglutination method described by Griffith¹². Agglutination of granular or self-agglutinating cultures was facilitated by digestion with trypsin, as described by Allison¹³.

The strains isolated from the 14 cases — 10 of scarlet fever and 4 of sore throat — and 16 contacts in Outbreak A agglutinated with type-specific rabbit antiserum prepared against Griffith's Strain 130 (Type 1). These streptococci grew as glossy colonies. The strains isolated from the 11 cases and 9 contacts in Outbreak B agglutinated with type-specific rabbit antiserum prepared against Griffith's Strain Franklin (Type 5). These streptococci grew as typical matt colonies. Both the Griffith Type 1 and Type 5 strains produced a toxin homologous with that of Strain N Y 5, as determined by toxin-antitoxin neutralization tests in rabbits^{14*}.

EPIDEMIOLOGY

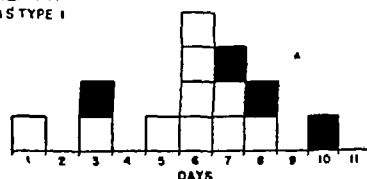
Outbreak A

The first outbreak occurred in a small country orphanage with 31 inmates, 26 of which were chil-

dren four to fifteen years of age. Several of them attended local schools where scarlet fever was prevalent. One of these, a nine-year-old boy, developed scarlet fever late in September, 1943. The original patient made an uneventful recovery, but 10 cases of scarlet fever and 4 of streptococcal sore throat occurred in the orphanage from November 7 to 16. The distribution of cases according to the day of onset is shown in Figure 1. Such a distribution suggests a common source, but this could not be established by the investigation.

Nose and throat cultures of cases and contacts revealed a Group A, Type 1, streptococcus as the

OUTBREAK A
GRIFFITH'S TYPE 1



OUTBREAK B
GRIFFITH'S TYPE 5

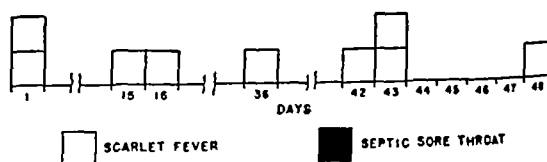


FIGURE 1 Day of Onset of Scarlet Fever and Sore Throat
Two missed cases are not included

causative agent. This organism was recovered in the first series of cultures from 7 cases and 15 contacts, indicating widespread dissemination of the causative organism among the inmates over a comparatively short interval of time. It is noteworthy that of 15 contacts who harbored the causative organism in the nose or throat, 10, all children, had positive Dick tests (Table 1).

The first cultures were taken after the scarlet-fever cases had received 1 gm. of sulfamerazine daily for five days. When it was discovered that a large proportion of the susceptible subjects (with positive Dick tests) harbored the etiologic agent, it was decided to administer prophylactic doses of a sulfonamide. Half a gram of sulfamerazine was administered once daily to all contacts for ten days. Subsequently, contacts with positive Dick tests were treated for an additional five days. Cultures taken at this time revealed that 6 persons — 3 patients and 3 contacts — still harbored a Type 1 streptococcus. Two of the patients had developed a minor complication — one a cervical adenitis and the other a nasal discharge. These 6 persons were then treated with a 2.5 per cent solution of sulfadiazine (Pickrell's solution) as a spray to the nose

*These toxins were prepared by Dr. Geoffrey Edsall, acting director of the Division of Biologic Laboratories, Massachusetts Department of Public Health.

and throat, administered five times daily for five days. Cultures taken after the spray treatment (twenty-one days after chemoprophylaxis was begun) revealed that Type 1 streptococci had disappeared from the entire group (Table 1). A carrier of Type 1 streptococci was disclosed in the final series of cultures two weeks later. Dick tests performed at that time revealed that a reversal from positive to

the beginning of the study are summarized in Figure 2, which also records the results of Dick tests and nose and throat cultures of the contacts. It was found that 11 healthy persons, including the teacher, carried Type 5 streptococci in the nose or throat. Of 14 contacts with positive Dick tests, 5 harbored the causative organism. Study of air-flow currents* revealed that 20 per

TABLE 1 Cultural and Dick-Test Status of Cases and Contacts in Outbreak A

Case No	Age yr	DIAGNOSIS	DICK TESTS*		TYPE OF HEMOLYTIC STREPTOCOCCUS					
			PRIMARY	SECONDARY	FIRST WEEK†	SECOND WEEK	THIRD WEEK	FOURTH WEEK‡	FIFTH WEEK	SEVENTH WEEK
1	10	Scarlet fever	+	—	1	1	1	1	0	19§
2	13	Scarlet fever	+	+	1	0	0	0	0	19§
3	13	Scarlet fever	+	—	1	1	1	1	0	0
4	4	Scarlet fever	+	—	1	1	0	0	0	0
5	4	Scarlet fever	+	—	0	1	0	0	0	1
6	6	Scarlet fever	+	—	0	0	0	0	0	0
7	6	Scarlet fever	+	—	0	0	0	0	0	0
8	3	Scarlet fever	+	—	0	1	1	1	0	0
9	5	Scarlet fever	+	—	0	0	0	0	0	0
10	8	Scarlet fever	+	—	1	1	1	0	0	0
11	13	Sore throat	+	+	1	1	1	0	0	0
12	13	Sore throat	+	+	1	1	0	0	0	6
13	7	Sore throat	—	—	0	0	0	0	0	0
14	12	Sore throat	—	—	0	1	1	0	0	0
15	12	Contact	+	+	1	1	1	0	0	0
16	15	Contact	—	—	1	0	0	0	0	0
17	10	Contact	+	+	1	0	0	0	0	0
18	10	Contact	+	+	1	1	1	0	0	0
19	15	Contact	—	+	1	0	0	0	0	0
20	15	Contact	+	+	1	0	0	1	0	0
21	12	Contact	+	—	1	1	0	0	0	0
22	13	Contact	—	—	1	0	0	0	0	0
23	11	Contact	+	—	1	0	0	0	19§	0
24	9	Contact	+	+	1	0	1	1	0	0
25	12	Contact	+	+	1	0	0	0	0	0
26	14	Contact	+	+	1	1	1	0	0	0
27	56	Contact	—	—	0	0	0	0	0	0
28	67	Contact	—	—	1	1	0	0	0	0
29	58	Contact	—	—	1	1	0	0	0	?
30	60	Contact	—	—	1	1	1	1	?	?
31	62	Contact	—	—	1	0	0	0	0	2

*Primary Dick tests done after onset of the first cases
†Patients had had oral drug for five days before the first series of cultures
‡First cultures after contacts treated for fifteen days with sulfamerazine (0.5 gm. daily)
§Weak cross agglutination with Types 4, 24, 26 and 29

negative had occurred in 1 of the contacts and in 10 of the patients (Table 1).

Outbreak B

The second outbreak occurred among 33 fifth-grade children in a single room of an elementary school with a total population of 495 children distributed among fourteen schoolrooms. Scarlet fever was reported from the involved room only. A total of 9 cases of scarlet fever occurred in this room from December 6, 1943, to January 24, 1944. Two additional cases were revealed during the course of the epidemiologic investigation. The dates of onset (Fig. 1) suggest transmission from patient to patient or from carrier to patient. Nose and throat cultures obtained from all 11 cases revealed a Group A, Type 5, streptococcus as the etiologic agent. The findings in the room at

cent of the air within the schoolroom was being recirculated by means of a unit ventilator. Streptococci were recovered from six of thirty-six blood agar plates that had been exposed for twenty-four hours on desks vacated by children who had developed scarlet fever, and from two cultures taken from dust that had collected on the ventilator fan. Of these eight cultures, two showed Type 5 streptococci. Of twenty blood agar plates exposed in an adjacent room where no scarlet-fever cases had occurred, hemolytic streptococci were recovered from three, none of these were Type 5. When it was discovered that a large proportion of the contacts were carrying a Type 5 streptococcus, chemoprophylaxis was begun in an attempt to protect the susceptibles. All children remaining

*We are indebted to Mr. C. P. Yaglou of the Harvard School of Public Health for the studies of ventilation.

in the room received 2½ per cent sulfadiazine in ethanolamine solution as a spray daily, once during the morning and once during the afternoon. Included in this group were 4 convalescent scarlet-fever cases, all with cultures positive for Type 5

Nose and throat cultures were taken from the family contacts of several of the scarlet-fever patients. Of 23 contacts examined (Fig 3), 13 had cultures positive for Type 5 streptococci. Five secondary cases, in none of which the patients at-

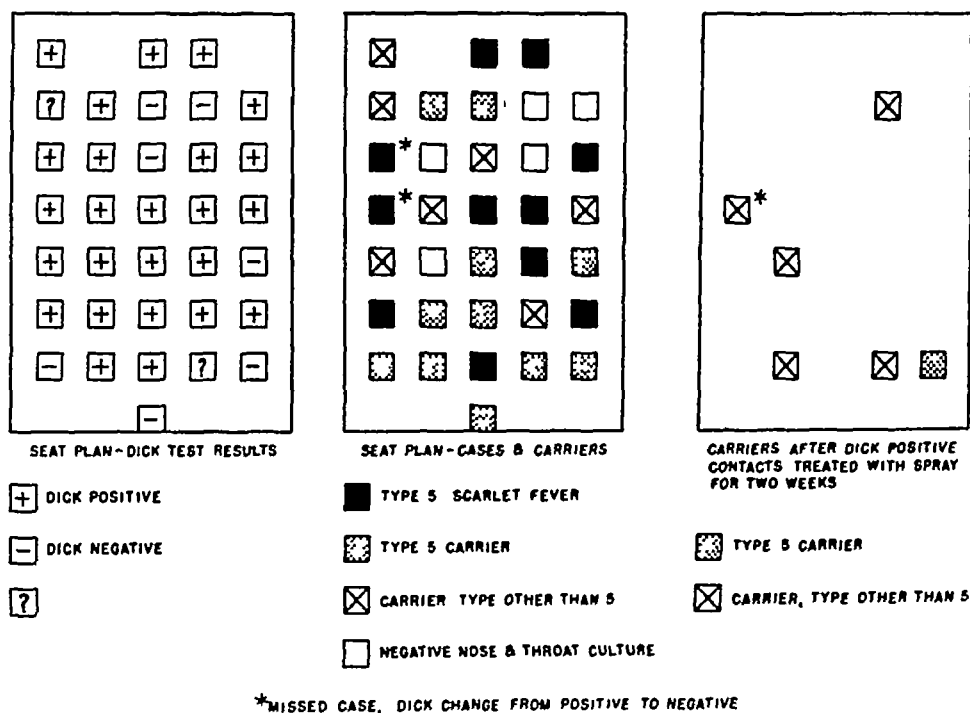


FIGURE 2 Data on an Outbreak of Scarlet Fever among the Children in a Schoolroom

streptococci. After seven days of spray treatment, a second series of cultures revealed that 4 contacts and 3 convalescent patients were still carrying a Type 5 streptococcus. During the second week, spray treatment was restricted to those children who had positive Dick tests in addition to those whose cultures were still positive for Type 5 streptococci. Table 2 indicates the number of carriers before and after spray treatment. It will be seen that after the second week only 1 healthy contact had a positive culture for the etiologic organism.

At the time that the last 4 scarlet-fever patients had been released from isolation and were about to return to school. Of these, 1, who had received chemotherapy early in the course of the illness, had negative cultures. The remaining 3 were still carrying Type 5 streptococci. To eliminate as many potential sources of infection as possible, the convalescent patients with positive cultures were given 1 gm of sulfadiazine daily for four days. At the end of that period and one week later the cultures were negative. Subsequent cultures of the entire group after two weeks and again after four weeks revealed the presence of Type 5 streptococci in the nose and throat of 4 of the convalescent patients. No new infections appeared in the schoolroom.

tended school, occurred among the family contacts of the 11 primary-infection cases. Type 5 strepto-

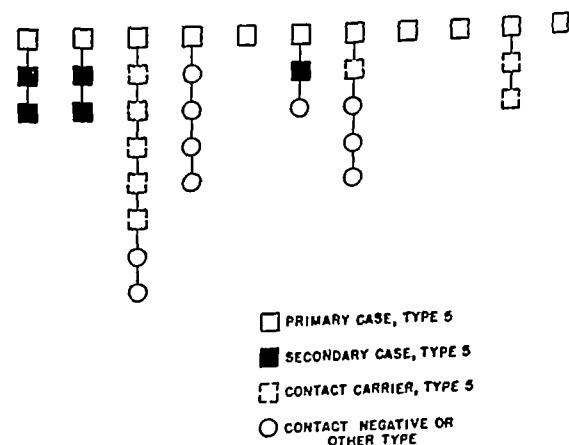


FIGURE 3 Diagram Showing the Spread of Hemolytic Streptococci among Scarlet-Fever Contacts

cocci were recovered from each of these secondary cases.

During the course of this outbreak a total of 25 cases of scarlet fever had occurred in the entire com-

munity Of these, 16 (64 per cent) were associated with the schoolroom outbreak Type 5 streptococci were recovered from a single sporadic case The remaining cases were caused by one of several other serologic types — Types 2, 1 and 6 in order of frequency

EFFECT OF CHEMOTHERAPY

Cases in Outbreaks

The duration of the postscarlatinal carrier state

patient who had received chemotherapy lost the causative organism before the second week of the illness A second had negative cultures after the fifth week Although subsequent cultures did not reveal the etiologic organism for an additional four weeks, there was a reappearance of the same type of streptococcus in the fifth week (the tenth week after onset)

Cases 6, 7, 8 and 9 in Outbreak B are worthy of mention These patients had received no sulfa-

TABLE 2 *Cultural and Dick-Test Status of Cases and Contacts in Outbreak B*

CASE No	DIAGNOSIS	PRIMARY DICK TEST*	TYPE OF HEMOLYTIC STREPTOCOCCUS									
			FIRST WEEK	SECOND WEEK	THIRD WEEK†	FOURTH WEEK	FIFTH WEEK	SIXTH WEEK	SEVENTH WEEK	EIGHTH WEEK	TENTH WEEK	ELEVENTH WEEK
1	Scarlet fever	+	5	5	5	5	5	0	0	?	?	?
2	Scarlet fever	+	5	5	5	5	5	2	0	0	5	0
3	Scarlet fever	+	5	5	5	5	5	0	2	2	0	2
4	Scarlet fever	+	5	5	5	5	5	0	0	0	0	0
5	Scarlet fever	+	5	5	5	5	5	0	0	0	5	0
6	Scarlet fever	+	5	5	5	5	5	5	0	0	0	0
7	Scarlet fever	+	5	5	5	5	5	0	17‡	0	17‡	0
8	Scarlet fever	+	5	5	5	5	5	0	0	0	0	0
9	Scarlet fever	+	5	5	5	5	5	19§	19§	19§	5	5
10	Scarlet fever	+	5	0	1	1	0	1	1	0	1	0
11	Scarlet fever	+	5	5	5	5	5	0	17‡	17‡	17‡	5
12 (teacher)	Contact	—	5	5	0	0	0	0	0	0	0	0
13	Contact	—	5	0	0	19§	0	0	0	0	0	0
14	Contact	+	0	0	19§	0	0	0	0	0	0	0
15	Contact	+	0	0	0	0	19§	0	0	0	0	0
16	Contact	+	5	0	0	0	0	0	0	0	19§	0
17	Contact	+	19§	0	0	?	?	0	0	0	0	0
18	Contact	+	0	0	0	0	?	0	0	0	0	0
19	Contact	+	1	1	0	0	0	0	0	19§	0	0
20	Contact	?	5	5	8	8	0	2	2	2	0	0
21	Contact	+	5	0	0	0	0	0	0	0	0	0
22	Contact	+	2	2	0	2	2	0	0	0	0	0
23	Contact	+	0	1	0	0	0	0	0	0	0	0
24	Contact	+	5	5	0	1	1	2	2	2	0	0
25	Contact	+	5	0	0	0	0	?	?	0	0	0
26	Contact	+	5	19§	0	19§	0	8	8	0	0	0
27	Contact	—	5	0	0	19§	0	?	?	0	0	0
28	Contact	+	0	0	0	0	0	?	0	0	0	0
29	Contact	+	0	0	1	0	0	?	0	0	0	0
30	Contact	?	19§	0	0	2	0	0	0	0	0	0
31	Contact	—	5	0	19§	19§	0	0	0	0	0	0
32	Contact	—	8	0	0	19§	0	0	0	0	0	0
33	Contact	—	19§	0	19§	0	0	0	0	0	0	0
34	Contact	—	5	5	5	0	0	0	0	0	0	0

*Secondary Dick tests could not be done

†First cultures after contacts treated for fourteen days with Pickrell's solution twice daily

‡Weak cross agglutination with Type 23

§Weak cross agglutination with Types 4 24 26 and 29

for the cases occurring in both epidemics showed striking differences

In Outbreak A the average duration of positive cultures for the sulfadiazine-treated cases was less than two weeks Nose and throat cultures of 6 cases were consistently negative after the third week In 1 case there was a reappearance of the causative organism after cultures had been negative for four weeks

The average duration of the convalescent carrier state in Outbreak B was at least eight weeks One

diazine preparation during their acute illness Following the administration of 1 gm of sulfadiazine daily for four days, in the fifth week after onset cultures promptly became negative for Type 5 streptococci In 3 cases, other types of streptococci not identified with this outbreak replaced the Type 5 streptococcus Here again, subsequent cultures of 1 of these patients disclosed a reappearance of the etiologic organism after a four-week interval during which it had not been demonstrable

Sporadic Cases

Studies of sporadic scarlet-fever cases revealed similar results (Table 3). Nose and throat cultures of 32 (84 per cent) of 38 untreated cases showed at the time of discharge the identical organism that had been present on admission. However, 10 (62 per cent) of 16 sulfathiazole-treated patients had negative cultures after the third week of illness, and 9 (69 per cent) of 13 sulfadiazine-treated ones had negative cultures after the same period of time. Pickrell's solution utilized as a spray in 13 cases produced negative cultures in 10 (77 per cent) at the conclusion of the three-week isolation period.

Although all three chemotherapeutic agents were equally efficacious in reducing the number of patients carrying the causative organism, subsequent cultures revealed that in a considerable proportion there was a reappearance of the initially isolated

eliminate streptococci from the nose and throat of the convalescent carrier.

Experience with several epidemics in schoolrooms suggests that multiple cases of scarlet fever due to a single type of hemolytic streptococcus are by no means infrequent.¹³ Frequently, investigation of contacts during these epidemics reveals the presence of chronic hemolytic-streptococcus carriers, some of whom are found to be either unrecognized cases or convalescent carriers who have returned to school following the expiration of the usual quarantine period.

In the epidemiology of scarlet fever, missed cases and convalescent carriers are far more important as sources of infection than is generally believed. The customary streptococcus-carrier survey does not attempt to differentiate the convalescent case and the healthy carrier. Such surveys will be more useful when an attempt is made to explain the

TABLE 3 Effect of Chemotherapy on the Streptococcus-Carrier State Following Scarlet Fever

Drugs	No of Cases	Types of Streptococci Isolated*	No of Cases with Positive Throat Cultures			Cases with Negative Throat Cultures on Discharge		Cases in which Original Type Reappeared 1 to 5 Weeks Later	
			First Week	Second Week	Third Week	No	Percentage	No	Percentage
Sulfathiazole	16†	1, 2, 19, 17, 8, 6	12	11	6	10	63	5	50
Sulfadiazine	13	2, 1, 8, 6, 5	13	6	4	9	69	5	80
Pickrell's solution	13	2, 6, 8, 17, 1	13	12	3	10	77	2‡	67
None	38	2, 1, 6, 8, 19	37	32	32	6	16	3	50

*In order of frequency.

†Hemolytic streptococci not isolated from 1 case during the period of isolation.

‡Of 3 cases studied.

streptococcus (Table 3). In 5 (50 per cent), of 10 sulfathiazole-treated cases, such a reappearance occurred at intervals ranging from one to five weeks after the cultures had become negative. Similarly, in 5 (55 per cent), of 9 patients who had negative cultures after treatment with sulfadiazine there was a reappearance of the etiologic streptococcus. Only 3 of the patients who had been sprayed with Pickrell's solution were studied after discharge from the isolation hospital. Reappearance of the causative organism was observed in 2 of these.

DISCUSSION

In both outbreaks the etiologic agent appeared to be successfully eliminated from the respiratory tracts of the temporary carriers. Whether the outbreaks were checked by this method is a matter of conjecture. Although a large proportion of the contacts had positive Dick tests, it was impossible to say that these persons were in addition susceptible to the streptococcus itself.

In a study of this type, temporary carriers must be differentiated from convalescent carriers. It was found that although sulfadiazine spray was adequate for the treatment of the healthy carrier, it did not

presence of streptococci in the upper respiratory tract by utilizing all available bacteriologic, clinical and epidemiologic knowledge.

Family studies suggest that children who acquire scarlet fever in school convey the infecting organism into the home, where it is dispersed among the contacts, a proportion of whom may develop scarlet fever or some other streptococcal infection.¹⁶ Also, in family units the carrier rate rises as a result of the introduction of a specific organism into the group by a scarlet-fever patient. Similar observations have been made during the course of institutional outbreaks of streptococcal infection.¹⁶ This factor may account for the high healthy-carrier rates associated with the types of streptococci that are causing scarlet fever in a community.

The frequent occurrence of late secondary cases among family contacts on the return to the home of patients cared for in hospitals is a well known fact. Similarly, in the schoolroom outbreak it was shown that with one exception each of the untreated patients who had returned to school still harbored the incriminated streptococcus in the nose and throat at the expiration of the three-week quarantine period.

Our observations suggest that the administration of sulfathiazole or sulfadiazine to scarlet-fever patients results in the development of a temporary period of so-called "cultural latency," during which the causative organism cannot be isolated from the mucous membranes of the nose and throat. After an interval of one to five weeks, however, there is a reappearance in the cultures of the streptococcus that had been isolated earlier in the course of the infection. In seeking an explanation for the observed period of "cultural latency," it may be pointed out that the fundamental mode of action of the sulfonamides appears to be bacteriostatic rather than bacteriocidal.¹⁷

The question arises whether this period of latency has any effect on the incidence of late secondary cases. Some data concerning this point were available at the contagious hospital where the sulfathiazole-treated cases had been studied. At this hospital 455 cases of scarlet fever had been treated routinely with sulfathiazole over a period of two years — 1942 and 1943. Examination of the hospital and board-of-health records revealed that following discharge of the primary cases from the isolation unit, 25 secondary cases — an incidence of 5.4 per cent — had occurred among the family contacts. From 1939 to 1941, inclusive, following the discharge of 398 hospitalized patients who had received no chemotherapy, 28 secondary cases — an incidence of 7 per cent — were reported among the family contacts.

The interval between the time of discharge of the primary case and the occurrence of the first case of secondary infection was established for each of the two groups. The average interval was 9.2 days for the treated cases and 12.6 days for the untreated ones. From the standpoint of the incidence of secondary cases and of the interval between the discharge of the primary case and the occurrence of the first secondary infection, there was no significant statistical difference between the two groups.*

These observations indicate that the period of "cultural latency" has little effect on the spread of scarlet fever. Additional studies have been undertaken to ascertain the effect of chemotherapy on a larger number of cases. The results of study of untreated cases emphasize the arbitrary nature of the isolation period in scarlet fever. Since the great majority of patients harbor the etiologic organism at the time of discharge from the isolation hospital, it is apparent that the customary three-week isolation period does not accomplish its purpose.

Although it has been demonstrated that the sulfonamides are of therapeutic value, there is little or no evidence that the routine use of chemotherapy has any effect on the incidence of late secondary cases. In this connection, the problems of drug sensitivity and drug fastness merit careful consideration. It

must be borne in mind that the sulfadiazine drugs have been most effective in the treatment of the fatal complications of scarlet fever. It would be unfortunate if their value for these secondary infections were impaired by the development of drug-resistant strains. From the point of view of controlling the spread of scarlet fever, there appears to be little justification for the routine treatment of patients with the sulfonamides.

SUMMARY

The epidemiologic investigation of two small outbreaks of scarlet fever, one occurring in an orphanage and due to a Type 1 streptococcus, and the other occurring in a schoolroom and due to a Type 5 streptococcus, presented an opportunity to study the effect of chemotherapy on temporary and convalescent carriers.

In both epidemics the utilization of small daily doses of a sulfonamide preparation — sulfamerazine in the first instance and sulfadiazine (Pickrell's solution) in the other — apparently reduced to a minimum the number of persons carrying the incriminated organism.

Studies among the families of children who acquired scarlet fever in the schoolroom outbreak revealed a spread of the causative organism to a large proportion of the family contacts, with the occurrence of several secondary cases.

A study of a group of untreated scarlet-fever patients showed that when discharged from isolation hospitals the majority carried the same type of streptococcus that was present on admission.

A large proportion of scarlet-fever cases treated with certain of the sulfonamides developed a temporary period of "cultural latency." In approximately half these cases, however, the original streptococcus reappeared in the cultures after an interval of one to five weeks.

A study of sulfathiazole-treated cases suggests that the period of "cultural latency" has no effect on the incidence of late secondary cases.

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HODGKIN'S DISEASE*

Report of a Case of the Mediastinal Type with Leukopenia and Terminal Atelectasis

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SINCE Hodgkin's¹ original description in 1832 of the disease known by his name, many papers have appeared in the medical literature that attempt to clarify both the etiology and pathology as well as the symptomatology of this illness.

So far as the etiology is concerned, the cause of the disease still remains unknown, although two main theories have been put forward to explain its origin.² The first holds that the changes in the lymphoid tissues are the result of an infection, the disease thus being a specific infective granuloma of unknown origin. The second theory, on the other hand, considers the alterations in the lymph nodes as neoplastic, thus placing the disease in the category of true neoplasms. The pleomorphism of the microscopic picture, consisting of necrosis with subsequent fibrosis, suggests an inflammatory lesion, whereas the local spread and the uniformly fatal outcome of the disease are characteristic of malignancy. The theory that Hodgkin's disease represents a special form of tuberculosis has been almost entirely disregarded.

Several pathological classifications have appeared, the most recent one, by Jackson and Parker,³ dividing the disease into three types: paraganuloma, granuloma and sarcoma. This division was made on the basis of two features, namely the presence in each of the so-called "Reed-Sternberg" cells and the transformation, in the course of time, of one type of the disease into another. According to these authors, Hodgkin's paraganuloma bears little or no resemblance to a true tumor, either in its histologic picture or its clinical course, but because of the complete lack of invasiveness, the lymphocytic infiltration, the often scattered, isolated Reed-Sternberg cells and the comparatively benign course, it is considered an infectious process. The same holds true for Hodgkin's granuloma, in which, according to these authors, the frequently scattered, isolated Reed-Sternberg cells, viewed

from the pathological standpoint, and the irregular bouts of fever, the marked anemia in absence of bleeding or widespread invasion of the marrow, the polymorphonuclear leukocytosis and the prominent and persistent tachycardia from the clinical point of view are more characteristic of an infectious process than of a tumor. Hodgkin's sarcoma, however, is considered by Jackson and Parker as a true neoplasm. This opinion is based on the uniformity of the cellular constituents, the aggressive, invasive nature of the process, the extremely short duration of life and the not infrequent finding of a large destructive tumor with comparatively few metastases.

So far as the symptomatology is concerned, great difficulties were encountered in dividing the disease into different types, because of the wide scope of the illness and its numerous diverse, protean symptoms. Most authors still accept Ziegler's⁴ plan, which divided the disease clinically into nine forms — acute, localized, general, mediastinal, larval or abdominal, splenomegalic, osteoperiostitic, atypical (gastrointestinal — Mikulicz's disease) and mycosis fungoides. It is beyond the scope of this paper to discuss all these forms, but it should be noted that, in spite of Ziegler's classification, there is often a clinical transformation from one of these types into another.

The following case is reported because of its unusual combination of clinical symptoms and the diagnostic difficulties it presented.

C. G., a 28-year-old man, was admitted with the chief complaint of severe vomiting of 2 weeks' duration. Two weeks prior to admission the patient started to vomit 2 hours after taking food and also experienced considerable midepigastric pain. There was also marked weight loss during this period. When admitted to the hospital he presented symptoms of partial intestinal obstruction and marked dehydration.

The past history revealed that the patient had been treated for peptic ulcers for the last 5 years. This type of treatment was undertaken on the basis of the clinical symptoms, which were fairly typical of a peptic ulcer, although repeated gastrointestinal x-ray studies failed to show any evidence of ulcer.

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The regime consisted of a moderate Sippy diet with the addition of alkali, antispasmodics and sedatives. The patient carried out this regime fairly conscientiously, and up until the beginning of the present illness showed no acute symptoms related to the gastrointestinal tract. A complete chest examination, including x-ray films, which was done 1 year before admission, was entirely negative. Six months prior to admission he was hospitalized for 2 weeks for a sprain in the lumbar spine, from which he made a complete and uneventful recovery. Otherwise the past history was uneventful.

The patient's father died of a leukemic condition, the exact nature of which could not be determined. The patient was married and had five children, all of whom were in good health. He had been working as a dispatcher in a war plant for over five years and had never been exposed to any chemicals, such as benzol.

Physical examination on admission showed a markedly dehydrated, poorly nourished man, presenting a clinical picture of partial intestinal obstruction. There was evidence of recent weight loss. Except for some tenderness in the right upper quadrant of the abdomen, the examination was negative. No masses were felt, and there was no enlargement of the liver or spleen, nor were there any palpable lymph nodes.

The urine was negative and had a specific gravity of 1.014. The red-cell count was 3,960,000 and the hemoglobin 65 per cent. The white-cell count was 3100, with 51 per cent polymorphonuclear leukocytes, 47 per cent lymphocytes and 2 per cent eosinophils. A slight polychromasia with anisocytosis was noted. A blood Hinton test was negative. The sedimentation rate was 23 mm in 1 hr (Wintrobe method). A blood culture was negative. The icteric index was 5.

A second blood examination, made 10 days after admission, revealed the red-cell count and the hemoglobin to be about the same as on admission, but the white-cell count had increased to 4700. The differential count was approximately the same as on admission. The reticulocyte count was 1.8 per cent, and the blood platelets numbered 350,000. A blood culture was again negative, and the sedimentation rate had decreased to 12 mm in 1 hr. A gastric analysis showed a faint trace of combined hydrochloric acid but no free hydrochloric acid in the fasting specimen. After histamine injection a faint trace of free hydrochloric acid appeared, but not enough for exact values to be ascertained. Daily stool examinations for occult blood revealed positive findings on four occasions and negative values on one. Agglutination tests for typhoid, paratyphoid and undulant fever were negative. The total serum protein was 7.2 gm per 100 cc, the albumin fraction being 4.5 gm, and the globulin fraction 2.7 gm. The urine was negative for Bence-Jones proteins.

One month after admission the white-cell count began to show abnormal values in the form of a definite leukopenia, ranging between 975 and 1700 cells, as determined by daily examinations. The differential count showed a neutrophilia, with lymphocytosis on several occasions, but at no time an eosinophilia. On two smears a large number of metamyelocytes and a few myelocytes were found, in addition to many degenerating white cells and basophilic stippling of the red cells. There were also moderate hypochromia, anisocytosis and polychromasia. Except for these two occasions, however, the differential count showed normal values relatively, in spite of the marked leukopenia. The red-cell count during this period varied between 3,000,000 and 3,500,000, and the hemoglobin between 55 and 65 per cent. The reticulocyte count varied between 3.8 and 9.4 per cent, probably as a response to liver therapy. The sedimentation rate ranged between 12 and 20 mm in 1 hour and the total protein values remained the same — 7.2 gm per 100 cc. The gastric analysis was repeated and again showed no free hydrochloric acid on the fasting specimen, but a slight trace appeared after histamine injection. The icteric index was again 5. A blood culture was negative for the third time. A sternal-marrow puncture on two occasions showed entirely normal smears, but microscopic examination of the bony tissue of the marrow showed definite atrophy and fibrosis. Repeated urinalyses were negative except for slight traces of albumin and bacteria in the sediment. Sputum examination was negative.

About 1 week before the patient's death, the white-cell count increased slightly, but steadily, finally reaching values

between 2500 and 3000, but the differential count remained the same. At the same time, the red-cell count dropped sharply until it reached 1,100,000. The hemoglobin also decreased gradually to 50 per cent. The platelet count, however, remained the same, as did all the other laboratory findings.

An electrocardiogram was negative, except for evidence of slight myocardial damage.

Two complete gastrointestinal series, including a barium enema, were performed 3 months apart, and both were negative. A gall-bladder series (Graham-Cole test) was negative. A flat plate of the abdomen and an intravenous pyelogram were negative. Complete x-ray examination of the long bones, skull, sternum and spine revealed entirely normal findings. Several chest x-ray films were taken, and up to 2 weeks of death were negative, at that time the chest plate for the first time showed complete consolidation of the right base involving the middle and lower lobes. A diagnosis of lobar pneumonia was reported by the roentgenologist. An x-ray film of the chest taken 5 days later showed complete consolidation of the entire right lung. The left lung was clear, and the heart was not displaced. A diagnosis of pneumonia and pleurisy with effusion was made. Another chest film taken 5 days later showed complete opacity of the right side, with no displacement of the heart. A slight increase of lung markings on the left was also reported.

On admission the patient presented the clinical picture of partial intestinal obstruction. He was unable to retain food and complained of severe cramplike pain in the midepigastric region. Following the subsidence of the obstruction he was able to retain a soft diet, but the midepigastric pain continued to be present 1 to 1½ hours after food intake. He also lost weight gradually. There was no fever.

Physical examination 3 weeks after admission revealed marked tenderness and rigidity in the right upper quadrant of the abdomen, the liver was palpable 2 fingerbreadths below the right costal margin. No lymphadenopathy, splenomegaly or tenderness over the splenic region was found, but there was some tenderness on palpation over the flat bones, especially over the sternum. The prostate was not enlarged, tender or nodular. Neurologic examination showed hypoaffective tendon reflexes and normal superficial reflexes. There were no sensory disturbances, and the vibration sense was normal.

The patient's condition remained practically unchanged during the 1st month of hospital stay, but he then began to lose ground, slowly but steadily. He started to run a low-grade remittent type of fever, which persisted for 3 weeks, when the temperature finally rose to 104°F and became sharply intermittent. He complained of severe headaches and again started to vomit. He became extremely weak and the tenderness over the flat bones, especially over the sternum, continued to increase in severity. On one occasion the spleen appeared to be palpable on deep inspiration and there was marked tenderness over the splenic region, which persisted until death. At no time, however, were there any palpable lymph nodes. The patient's general condition rapidly deteriorated and he lost markedly in strength and weight.

Two weeks prior to death, the patient suddenly developed an increasingly severe cough, productive of a small quantity of white mucus, associated with this was bilateral wheezing, especially marked over the right side of the chest. In spite of the x-ray report of lobar pneumonia, a clinical diagnosis of obstruction of the right lower main bronchus producing atelectasis of the right lower and middle lobes was made. Three days later there was a complete absence of breath sounds over the right lung with some expiratory wheezing rales on the left side. Clinically there was slight dyspnea and cyanosis, and the cough decreased in severity. This condition continued for 1 week, when the dyspnea markedly increased and the patient began to expectorate large amounts of thick, greenish mucus. Chest examination revealed many expiratory wheezing rales in both lungs and moist bubbling rales at both bases. He then developed for the first time signs of mediastinal pressure — severe difficulties in swallowing and hoarseness. He died 48 hours later.

Treatment consisted in the beginning of supportive measures such as glucose, saline and amino acid infusions, alkali and antispasmodics. As soon as he was able to retain food, he was given small frequent feedings. After the diagnosis of hypochlorhydria was established, he received dilute hydrochloric acid before meals. The diet was high in carbohydrates and proteins and rich in vitamins. The hypochromic anemia

in the beginning of the illness was combated with iron and crude liver extract. Because of the intermittent type of temperature, the patient was given a course of penicillin, receiving a total of 1,000,000 units intramuscularly in a period of 10 days. This, however, had no effect on the fever. He also received a course of Pentnucleotide (10 cc intramuscularly three times a day for sixteen injections) because of the leukopenia and neutrophilia. This, too, was entirely unsuccessful. He also received eleven 500-cc blood transfusions over a period of 2 months. Otherwise the treatment was purely symptomatic and supportive.

Autopsy

At autopsy the right pleural cavity contained 2500 cc of straw-colored fluid. The right lung was entirely collapsed, and the left lung, as well as the heart, was markedly displaced to the right. At the root of the right main bronchus there was a large tumor mass, measuring 6 by 4 by 2.5 cm. There were also six peribronchial lymph nodes, of pea to bean size, around the root of the right main bronchus. The liver was markedly enlarged, weighing 2020 gm, but the cut surface was normal. The spleen was somewhat enlarged, weighing 280 gm, but showed a normal cut surface. No enlarged abdominal or superficial lymph nodes were found. The sternal marrow appeared to be paler than usual. Microscopical examination of the lymph nodes showed many typical Reed-Sternberg giant cells, and the sternal marrow again was atrophic and fibrotic. The liver showed a mild degree of amyloidosis. The spleen appeared to be normal. **Diagnosis: Hodgkin's disease.**

DISCUSSION

The data derived from the history of this case, as well as the physical findings and the clinical course of the disease, permitted the diagnosis of Hodgkin's disease, which was later confirmed by autopsy findings. Not until two weeks prior to the patient's death, however, did the clinical picture become clear enough to permit a definite diagnosis of this disorder. Up to that time there were many findings suggesting Hodgkin's disease without being pathognomonic of this disorder. A brief review of the clinical course will demonstrate the diagnostic difficulties in this case.

The prodromal symptoms were related to the gastrointestinal tract. In spite of repeatedly negative x-ray findings, the clinical symptoms were so typical of a duodenal ulcer that the patient's physician felt justified in putting him on an ulcer regime. The fact that Hodgkin's disease may be preceded by gastrointestinal disorders was stressed both by Rolleston⁵ and by Bramwell⁶ as early as in 1909. In this case the gastrointestinal disorders finally became severe enough to produce a picture of partial intestinal obstruction, for which the patient was originally referred to the hospital. During the first weeks of his hospital stay, the clinical picture was characterized by generalized weakness and loss of weight, so that at one time a diagnosis of pulmonary tuberculosis was considered. This was ruled out, however, by repeated chest x-ray and laboratory examinations.

Although from the etiologic point of view tuberculosis is still favored by some investigators, there is general agreement that, clinically, tuberculosis follows rather than precedes Hodgkin's disease. This position was further strengthened by Ziegler's⁴ investigations, showing that in 25 per cent of patients

with Hodgkin's disease the terminal picture was that of miliary tuberculosis. According to Jackson and Parker,³ generalized weakness and loss of weight, for which no cause can be found, are not infrequently the first symptoms and may be most difficult ones to evaluate. The fact that Hodgkin's disease in its initial stage may be marked by the most diverse symptoms and signs was also stressed by Jackson and Parker.

To the prodromal symptoms of gastrointestinal disorders, generalized weakness and loss of weight might be added in this case the hypochlorhydria of the gastric juice and the mild hypochromic anemia, findings that, according to Ewing,⁷ are not infrequently noted and may dominate the clinical picture for some time. Fever occurred fairly late in this case. At first it was of the remittent type, without, however, ever resembling the typical Pel-Ebstein fever. Later it became sharply intermittent, suggesting a more or less septic condition. Repeated blood cultures, however, were negative, and a course of penicillin produced no changes.

The blood picture was both bizarre and puzzling. At first there was a mild to moderate hypochromic anemia, which at times showed a tendency toward the pernicious type, but which responded fairly well to liver and iron therapy, as evidenced by the gradual increase in reticulocytes. Whereas the red-cell picture appeared to be reasonably stable, the white-cell count showed a marked leukopenia which continually increased in severity. On several occasions a neutrophilia was also present, which, however, resisted treatment with Pentnucleotide. On two occasions young white cells were also found, but they were not persistent and on subsequent smears were absent. The blood platelets were normal. At no time was there an increase in eosinophilic cells, which some authors, among them Bunting,⁸ describe as one of the most significant diagnostic signs in Hodgkin's disease. One week prior to death there was a slight but steady increase in the white cells, whereas the red-cell count dropped markedly. Repeated blood transfusions were ineffective. A smear of the sternal marrow, which is also considered to be a helpful diagnostic procedure, appeared normal and did not clarify the clinical picture.

Other diagnostic procedures, such as complete gall-bladder and kidney studies, as well as x-ray examination of the long and flat bones, agglutination tests and numerous blood chemical tests, revealed normal values.

The physical signs were extremely vague. Except for a progressing hepatomegaly, the findings were practically nil until two weeks prior to death. There was no palpable splenomegaly, except for one occasion when the spleen seemed to be palpable on deep inspiration. Superficial lymphadenopathy was absent during the entire course. The tenderness over the flat bones, especial

sternum, and over the splenic region, should, however, be mentioned. Although hepatomegaly is mentioned by many authors as a fairly consistent finding in Hodgkin's disease, the occurrence of splenomegaly and superficial lymphadenopathies appears to be a much more frequent finding both in Hodgkin's granuloma and in Hodgkin's sarcoma and seems to be fairly pathognomonic of these two types, even the mediastinal form (Jackson and Parker,³ Ewing,⁷ Boyd,² Cecil⁹ and others)

A striking change in the clinical picture appeared two weeks before death. Then for the first time, mediastinal-pressure symptoms occurred, such as atelectasis of the right lung due to compression of the right main bronchus, difficulties in swallowing and hoarseness. This picture appeared to be fairly consistent with that described by other authors as typical of the mediastinal type of Hodgkin's disease. Up to that time, as already mentioned, the clinical picture was characterized by vague protean findings, some of which were suggestive but not pathognomonic of this disorder.

SUMMARY

A case of Hodgkin's disease, mediastinal in type and characterized by an unusual combination of prodromal symptoms and signs, is described, and the clinical course and the laboratory and autopsy findings are discussed.

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MEDICAL PROGRESS

PHYSIOLOGY

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THE re-examination of established principles often proves to be as effective a means of progress as the exploration of new fields. This is especially likely to occur in those instances where the weight of long tradition or great authority and the superficial appearance of reasonableness have combined to discourage the critical analysis of a doctrine. The demand for re-evaluation within recent years of two well buttressed concepts may therefore be viewed as important indications of progress in physiology and medicine. In both, which are discussed in the first two sections below, revision of basic physiologic tenets is involved, along with reconsideration of means of treatment. The first instance concerns the physiologic processes that participate in the production of edema in congestive heart failure, which have required renewed study in the light of revised methods of treatment. The second has to do with clinical observations on the abuses of recumbency and bed rest, which point to the need for more adequate data on the physiologic changes that occur in these circumstances, particularly in the aged and obese.

EDEMA IN CONGESTIVE HEART FAILURE

The subject of edema in congestive heart failure has been reopened through the examination of the value of restriction of fluid and salt in studies in which the two factors were varied separately.

Schroeder¹ studied 23 patients with congestive heart failure in whom restriction of salt intake to approximately 10 gm daily was sufficient to establish diuresis. When, in these circumstances, water intake was increased, edema was not increased. Occasionally, diuresis increased when added water was taken, and diminished with restriction of fluids. Schroeder concluded that restriction of salt is an important feature of the regime in congestive heart failure, whereas restriction of water is not essential.

Similar conclusions were reached by Proger, Ginsberg, and Magendantz,² who gave 4 patients recovering from congestive heart failure 10 to 12 gm of salt daily in addition to a dietary intake of 5 to 7 gm. Within four to eight days these patients developed a clinical picture indistinguishable from congestive heart failure, which was remedied by digitalis. Three

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patients were permitted to increase their fluid intake to 3000 cc daily without increase in salt intake. In none of these were there any noticeable harmful effects.

Finally, Schemm^{3,4} has shown that water has valuable diuretic properties, and that when water in excess of daily requirements is given, especially when sodium is moderately restricted and an acid-ash diet consumed along with moderate amounts of dilute hydrochloric acid or ammonium chloride, edema and other fluid accumulations disappear and the symptoms of congestive failure are relieved. Edema of other origins appears also to be favorably influenced. Fluid intakes as high as 5000 to 8000 cc a day have been employed successfully in such treatments. Presumably a high water intake is effective because it provokes an active diuresis, even in badly damaged kidneys, in the course of which excess salt is lost even though the urine is extremely dilute. Reduction in the salt content of the body fluids results in further loss of water to maintain osmotic equilibrium, with the net result that fluid is lost in greater volume than the ingested water.

These studies, which call attention to the role of salt and water accumulation as an important factor in the edema formation in congestive heart failure, also suggest that such accumulations may in fact precipitate the attack of failure. This is confirmed by the recent studies of Warren and Stead,⁵ who found that resumption of a normal salt intake and an additional 12 gm salt daily by two patients who had recovered from failure on a low-salt and diuretic regime led to typical attacks of congestive heart failure. The plasma volume increased prior to the onset of failure, but the venous pressure did not rise beyond the control range. The authors are therefore inclined to view the increased retention of salt and water, followed by an increased plasma volume, as the primary events in the collection of edema, and to discard the conventional theory that the accumulation of fluid results from increased venous pressure, or tissue anoxia, in heart failure.

Evidence that tissue anoxia cannot be responsible for edema formation is presented in another report by the same authors,⁶ in which it is shown that the protein content of edema fluid is not abnormally increased, nor is fluid obtained in patients with frank tissue anoxia, whereas the protein content of fluid collected after prolonged elevation of venous pressure is markedly elevated. The accumulation of salt and water is credited, instead, to a deficient renal excretion. This in turn may be due to excessive production of adrenal cortical hormones or to altered renal circulatory dynamics. The latter appears to be the most reasonable. The following sequence of events is then presumed to occur: failure of cardiac output, failure of renal circulation and consequent failure of salt excretion, water retention, increase in capillary pressure as the result of the augmented plasma volume, and consequently, in-

crease in extracellular fluid or edema. The increased venous pressure is thus viewed as the *result* of retention of salt and water — not the *cause* of it.

From an *a priori* standpoint this account fails to be completely satisfactory, depending as it does on the establishment of conclusive evidence that plasma volume does in fact increase before venous pressure is raised. It is difficult to accept the suggestion that the heart fails enough to derange the circulation in the kidneys before the venous pressure rises. It is generally assumed that the first reaction of the failing heart is to maintain a normal output through the operation of Starling's law of the heart, whereby the residuum of blood left in the ventricle by an incompletely effective systole is added to the normal diastolic inflow to distend the heart and thus to increase stroke volume to the point where a normal output is maintained at the expense of a slight increase in venous pressure. Failure begins when this mechanism is no longer successful, and increased filling is followed by diminished output. Thus, adding to blood volume in a heart at the point of failure precipitates failure, whereas reducing the volume, as by venesection or pooling of blood behind tourniquets, actually improves cardiac output by reducing the diastolic overload.

PHYSIOLOGY OF REST

Under the stress of an increasing demand for hospital and nursing care, one of the most firmly established of all therapeutic principles is being subjected to critical scrutiny. In the light of this re-examination, the doctrine of rest as a curative measure is seen to have certain important limitations, a number of which are brought out in a recent symposium⁷⁻¹¹ and in subsequent reports.¹²⁻¹⁴ The discussion is opened by Harrison, who recalls that John Hunter lived possibly twenty and certainly eight active and productive years after the first symptoms of coronary arterial disease, whereas James Mackenzie survived his initial cardiac attack by seventeen years, during fifteen of which he continued to play golf. He then reviews experiment carried out with Thomas,¹⁵ in which the survival rate was studied in rats after damage was inflicted on the myocardium by burning the left ventricle. In rats whose activity was restricted to approximately 10 per cent of that of unrestricted controls only 7 survived out of 49, whereas 21 out of 41 survived in the control group. Unconfined rats resumed normal activity in five days, as shown by their optional use of a treadmill in the cage. Forced, strenuous exercise (swimming) failed to influence mortality if it were not begun before forty-eight hours after the cardiac trauma. From these experiments the authors concluded that physical activity within the range of tolerance may be more beneficial than complete rest. They call attention, however, to the obvious fact that restraint, even though it may reduce skeletal muscular activity,

can hardly be termed rest, and it is highly uncertain that the cardiovascular load under these circumstances is in any measure diminished. This may be comparable to the patient who is forced by the physician to maintain an "unhappy recumbency" instead of a "happy sitting." Harrison lists the following as advantages to be sought in prolonged bed rest: a decreased liability to rupture of the heart, a better circulation to the brain during the period of circulatory collapse, and a firmer and smaller scar. The following are cited as disadvantages: the tendency to the formation of pulmonary edema, a diminished circulatory velocity, with a consequent tendency to intravascular clotting, and the development of hypostatic pneumonia, particularly in elderly people.

Levine cites as advantages of bed rest a diminished metabolism, a slower heart rate and a lower blood pressure, all of which diminish the work of the heart or improve its efficiency. On the contrary, the improved venous return associated with recumbency increases the cardiac output by some 25 per cent and tends to counterbalance the gains noted above. It is recognized that attacks of cardiac asthma are more frequent at night after several hours of recumbency, and their victims often learn to overcome them by sitting at the edge of the bed with the feet dependent. By this process, the fluid in the lungs is diminished and the venous blood is pooled in the dependent limbs, thus relieving the overdistended heart and permitting it to contract more efficiently. Even when the patient cannot sit up, it may be possible to carry out both active and passive limb exercises, and to elevate the head of the bed to begin to condition the cardiovascular system for the ultimate resumption of the upright position.

There appears to be general agreement that after surgical operations, particularly those involving the pelvis and abdomen, venous return from the limbs is delayed and serves as the basis for embolus formation in the small veins and venules of the dependent portions of the limbs, particularly in the obese and aged.¹⁶⁻¹⁹ Elevation of the limbs and exercise, especially the latter, markedly decrease the foot-to-carotid-sinus circulation time.^{16, 17} Walking soon after operation has been advocated as a measure to minimize postoperative thrombosis. Other advantages of early walking after surgery have been suggested as follows: improved gastrointestinal function, with lessened incidence of abdominal distention, improved muscular strength and absence of asthenia, which lead to a more rapid resumption of full activity, more rapid healing of the wound, improvement in morale, and economy in hospital beds and nursing care and in the cost of illness to the patient.

Dock emphasizes that bed rest is far from physiologic, involving long periods in the dorsal recumbent posture, usually with sedation to suppress the normal tendency to change frequently, and diminished

vital capacity and tidal volume. Unless specifically warned against it, the patient will many times a day repeat the Valsalva experiment (taking a deep breath, closing the glottis and contracting the expiratory muscles), when on the bedpan, expelling flatus or moving upward in bed. This maneuver places a great strain on the cardiovascular system, and often causes sudden death after myocardial infarction.

The symposium closes with a discussion of the psychosomatic aspects of rest, calling attention to the fact that the symptom of fatigue is only in rare cases at all related to exhaustion of muscular energy, but rather stems from an inability to direct energy output into properly balanced creative and destructive outlets. Therapy must therefore aim to utilize rather than to blockade the available energy of the patient.¹¹

It is obvious that these objections are directed not so much at the doctrine of rest itself as against abuses and misconceptions of the principle. Enforced muscular inactivity does not constitute rest, and may in fact prevent rest. Mental rest is often achieved by a combination of physical activity in a proper environment. Various operations of orthopedic surgery may effectively place a fractured bone at rest without at the same time depressing the functions of nearby joints and muscles. The complete bed rest of the patient with tuberculosis is accompanied by conscious or unconscious psychotherapy aimed at allaying anxiety and arousing a desire to carry out the treatment in every detail.¹⁴ Rest must therefore be prescribed, like any other therapeutic measure, with a clear idea of the aims sought by its employment and of its harmfulness when employed excessively and inappropriately. "Whenever we put a patient to bed," advises an editorial in the *British Medical Journal*,²⁰ "we should ask ourselves what we hope to achieve, and it must be something more than a tidy ward, a convenience for examination or a substitute for a convalescent room."

Closely associated is the problem of limitation of exercise in chronic illnesses, such as rheumatic fever, in which the decision may lie between a life of semi-invalidism and a virtually normal existence. Here the report of Kohn and McEldowney²¹ may serve as a guide to the extent to which persons with seriously impaired hearts may lead normal lives. The study concerns the fate of 233 former pupils of a special school for children who, because of disease, accident or congenital deformity, could not attend a regular school with "safety and profit." Eighty-five per cent had rheumatic heart disease, and 9.4 per cent suffered from congenital lesions of the heart. Twenty-five per cent had died, and 20 per cent had had recurrences of rheumatic fever. Of 130 pupils re-examined between the ages of seventeen and thirty-three years, only 5 per cent had never worked or were not working at the time of re-examination. Thirty-two women had married, and

of these, 14 had had one child, 3 had had two, and 2 had had four, in no case had the heart lesion affected adversely the pregnancy or labor. Fifty per cent of the women were doing their own housework, and many were performing heavy work.

It is obvious that, despite the seriousness of their heart disease, a majority of the persons included in the study had been able to enjoy, within their limitations, active and productive lives. Whether the mortality within the group would have been any less had their activity been more rigorously curtailed is open to question, but it is probable that the mortality in this group of patients was an indication of the seriousness of the heart disease, and might well have been as great if they had been receiving sanatorium care as semi-invalids during the whole period of the study.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31371

PRESENTATION OF CASE

A fifty-year-old widowed chauffeur was admitted to the hospital because of progressive anorexia, weakness, malaise and weight loss.

Sixteen years before admission the patient had had an acutely inflamed gall bladder drained. Seventeen days postoperatively he was discharged with a small draining sinus, which had continued to drain creamy yellow to green purulent material up to the time of admission. The drainage was intermittent, with frequent periods of several days during which the sinus tract closed. Within a few days there invariably followed a short period of local discomfort

and often pain, which was followed by reopening of the sinus and profuse drainage for a few days. Approximately one year after the operation, while doing heavy work, an orange-sized hernial mass suddenly appeared at the site of the operative scar. This hernia had never been painful and had not increased in size. Five years before admission he had had "pneumonia," which was treated at home. The patient had otherwise been entirely well until about two years before entry, when he began to feel sluggish, had no energy and lost ambition and interest in his work. He began to lose his appetite and weight. One year before admission he began to have mild attacks of "asthma," which became worse, two months before admission he was admitted to another hospital because of a severe attack. There had been no hemoptysis. He was discharged after eleven days, feeling considerably improved. Since that time he had continued to grow weaker and more exhausted. He had had occasional night sweats for an undetermined period of time.

Twelve years before entry his wife died after sanatorium care for tuberculosis of the sacroiliac joint. An eighteen-year-old daughter was living and well.

As a youth he had worked for several years in a dusty cardboard-box factory. Two years before admission he had worked for several months in a boiler room shoveling soft coal. He had had a mild chronic "cigarette cough" for about ten years, which im-

*On leave of absence.

proved when he stopped smoking three months before entry.

Physical examination revealed a poorly nourished, well developed, pale man with signs of recent weight loss. There was no lymphadenopathy. The chest was barrel shaped and showed diminished expansion. There were moderately fine rales at both bases posteriorly, extending higher on the right side. In the axillary line bilaterally there were some high-pitched musical rales. The heart border was not percussible, but the heart sounds were of fair quality. A blowing Grade 2 apical systolic murmur was heard.

The temperature was 98.6°F, the pulse 115, and the respirations 20. The pulse soon returned to about 90. The blood pressure was 100 systolic, 70 diastolic.

Examination of the blood showed a red-cell count of 4,000,000, with 80 per cent hemoglobin, and a white-cell count of 10,700, with 74 per cent neutrophils, 12 per cent lymphocytes and 14 per cent monocytes. The urine was acid, with a specific gravity of 1.015, a trace of bile and a rare white cell. A sputum specimen showed no tubercle bacilli. The stool was brown, and guaiac tests were positive.



FIGURE 1 *Roentgenogram of Chest*

but was not transmitted to the axilla. The abdomen was scaphoid, with an old operative scar in the right upper quadrant. At each end of the scar was a depression, the lower one having some dried exudate around it. To the right of the scar opposite its midpoint was a firm movable mass in the abdominal wall, this could not be reduced. On coughing, other viscera herniated into the pouch and lodged beside the permanent mass. Distinct epigastric tenderness and spasm were more marked on the right than on the left. No other masses were felt. One observer noted right pleural-angle tenderness.

Tuberculin tests in dilutions of 1:100,000 and 1:10,000 were negative. A blood Hinton test was negative.

X-ray films of the chest showed both lungs to be involved in a grossly nodular process, with a network of increased density connecting the more miliary nodules (Fig. 1). In addition there were areas of emphysema in the right lower lung and a few rarefactions suggesting cavities in the upper lung fields, particularly on the right. The heart was small but otherwise not remarkable. An electrocardiogram was consistent with coronary heart disease.

The serum nonprotein nitrogen was 36 mg per 100 cc with subsequent lower values, and the total protein 7.8 gm, with an albumin-globulin ratio of 0.88, the chloride was 98.0 milliequiv per liter, and one week later 85 milliequiv. The prothrombin time was 30 seconds (normal, 18 to 20 seconds). An oral Graham test was tried but the dye failed to pass the pylorus and outlined a distended stomach.

The patient was extremely weak and constantly tired. On the fifth hospital day the temperature became elevated and remained between 100 and 102°F for four days. Thereafter for about a week the oral temperature was between 97 and 98°F. On the sixth day he had an episode of what was thought to be paroxysmal auricular tachycardia, with a pulse rate of 160, which reverted to normal rhythm spontaneously in about twelve hours. A gastrointestinal series on the sixth hospital day revealed a normal esophagus. The stomach was atonic and contained fluid and retained food. Fluoroscopically there was thought to be a shallow ulceration on the lesser curvature just below the angulus. After transient prepyloric spasm the duodenal cap filled out well and appeared normal. The upper small intestine was not remarkable. The diaphragm moved equally well on both sides. Two days after the gastrointestinal series a gastric lavage yielded large amounts of barium. At that time numerous rales were heard throughout the chest and the patient stated that the lavage made him short of breath. A sputum culture was negative for beta-hemolytic streptococci and pneumococci.

On the eleventh hospital day the patient began to cough up blood-tinged sputum and a few particles of what appeared to be necrotic tissue. Frequently repeated smears for tubercle bacilli were negative, and a pathological examination on the sputum sediment revealed no tumor cells. A gastroscopy on the fifteenth day showed superficial gastritis with multiple erosions. The patient was relieved by daily gastric aspirations after the twentieth hospital day. He then appeared to have repeated attacks of pyloric obstruction, and approximately 1000 cc of foul-smelling, dark-brown, guaiac-positive, thick fluid was obtained with each aspiration. On the twenty-first hospital day the temperature, pulse and respirations began to rise, the temperature fluctuating between 100 and 103.5°F.

On the twenty-second day the patient became markedly dyspneic and apprehensive. The abdomen was distended. Peristalsis was present. The spleen was not felt. The liver was thought to be large. The blood chloride was 77 milliequiv per liter, and the total protein 4.5 gm per 100 cc. A van den Bergh test was 0.9 mg per 100 cc direct, and 1.2 mg indirect. On x-ray examination the appearance of the chest had not changed appreciably.

The patient became progressively weaker, more

dyspneic and ashen-gray despite an oxygen tent. His lungs were filled with rales, and he expired on the twenty-fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR JOHN W. CASS: The initial statement in this man's history makes one think of cancer of the stomach more than anything else. If cough were added, one would think of tuberculosis. The post-operative story is that of a patient with a residual empyema of the gall bladder, a draining sinus and the subsequent development of a ventral hernia. The history indicates a transition into a progressive illness, with localization in the chest as well as in the abdomen. The asthma by itself is not significant, since it could have been a symptom of a general disease. A malignant lesion of the chest is not uncommonly ushered in by attacks of asthma, and tuberculosis is not infrequently accompanied by asthmatic attacks.

We learn that there was a family history of tuberculosis, which suggests that perhaps the whole story was accounted for by tuberculosis. Contact is the one thing that one searches for, and here it can be established.

I know of no occupational hazard connected with a cardboard-box factory or with shoveling soft coal.

The physical examination again localizes the disease to the chest and to the abdomen. It brings into the picture a mass, which was not the hernia and which was not related to the sinus tract. The laboratory work indicates an obvious secondary anemia. The blood smear showed 14 per cent monocytes, which is not helpful by itself but is suggestive of tuberculosis. The trace of bile in the urine we have to accept as a pathological finding that incriminates the liver. The tuberculin tests are interesting. Negative tests with dilutions of 1:100,000 and 1:10,000 are rare in an adult of fifty, but in these dilutions they cannot be considered negative. The test should have been done with a dilution of 1:100. A negative tuberculin test in a man of this age is so rare that one might suspect he had some form of tuberculosis in the terminal stage.

May we see the x-ray films?

DR GEORGE W. HOLMES: There are two obvious things in this man's chest. He has a wide antero-posterior diameter and a low diaphragm—the characteristic appearance of an emphysematous chest. In addition he has a diffuse process that involves both lungs, the right more than the left. There is a suggestion of a cavity in the right apex. It is not definite enough, however, for me to say that it is a cavity, so that I am not particularly helpful. If it is a cavity, we have to consider carcinoma, tuberculosis and silicosis, although I should think that the last was unlikely.

DR. CASS: The x-ray report says "miliary nodules." Are they nodules or tiny cavities?

DR. HOLMES: I suppose they meant small nodules. I do not recognize that as a customary expression.

DR. CASS: Are they blebs or cavities?

DR. HOLMES: I do not know. Part of the chest is blurred, but there is probably some fluid in the pleural cavity.

DR. CASS: In the lateral films is there any evidence of bone change?

DR. HOLMES: No.

DR. CASS: There was a gastrointestinal series mentioned in the protocol.

DR. HOLMES: The films are not helpful.

DR. CASS: There was a statement about previous ulceration.

DR. HOLMES: I think that we have to take that for what it is worth. I am not able to demonstrate anything on the films. It was a fluoroscopic note.

DR. CASS: So the x-ray picture is that of a nodular, miliary process, not one of small cavities. The presence of a large cavity is questionable. The likeliest diagnosis is tuberculosis or a malignant neoplasm, pneumoconiosis or sarcoid being rather poor bets.

The nonprotein nitrogen was normal, which is surprising in a man so ill. The total protein was high and the albumin-globulin ratio was low when he came in. Later, the low protein and increased prothrombin time suggest intrinsic liver damage.

The paroxysmal auricular tachycardia does not help. There is no evidence that we are dealing fundamentally with a heart condition. Dr. Holmes says that we have to accept the statement that there was a gastric ulceration, but the most information we get is that there does not seem to have been any gross intrinsic disease of the stomach. There was ulceration, but it was not characteristic enough to make one think of tumor.

A real but unsuccessful effort was made to find acid-fast organisms. There was no evidence of tumor cells, at least in a single specimen. Gastroscopy helps in making us think that we are dealing, so far as the abdomen is concerned, with obstruction of the stomach. It could have been due to a pathologic process close to the pylorus or it could have been secondary to the hernia. In general the abdominal situation seems more compatible with tumor than with tuberculosis.

In the terminal days of the patient's course there was a marked change in the blood chemical findings, which is again compatible with a good deal of intrinsic liver disease. But we are dealing with a patient with extreme debility and malnutrition, and the laboratory work may not be too significant. It is important that there was no significant change in the x-ray films of the chest.

In summing up the situation, it seems to me that the picture is that of a wasting disease with localization both in the chest and in the abdomen, and

that in the beginning the difficulty was chiefly in the liver. So far as the chest is concerned, there was a diffuse nodular miliary process. The tuberculin test was negative, at least in dilutions of 1:10,000, as were sputum studies, so that the process in the chest is more compatible with tumor than with infection. I did not mention actinomycosis. That does give a nodular appearance, but it seems to me that the evidence narrows down to tuberculosis or tumor. So far as the abdomen is concerned, there were positive findings of gall-bladder empyema, with a draining sinus, a large liver, no jaundice and laboratory studies indicating a good deal of intrinsic liver damage. The pyloric obstruction, so far as we can tell, was extrinsic and could have been due to pressure from a mass in the region of the gall bladder or bile ducts. There may have been a rupture of the abdominal process into the chest, so that from a diagnostic point of view, we have to decide, first, whether we are dealing with tumor or infection and, second, whether there were two diseases.

It seems to me that if we can logically connect the two it is safer to make one diagnosis than to make two, and the weight of evidence seems to me to be in the realm of a malignant tumor. If so, where did it lie? We know that in patients with chronic draining sinuses for this length of time malignant degeneration is liable to develop in the sinus tract or gall bladder. Malignant disease in these areas usually metastasizes to the chest. If the process in the chest was nodular, it is compatible with metastatic malignancy, although one cannot rule out tuberculosis, particularly that of the miliary type. By far the safest diagnosis is malignant tumor developing in the region of the gall bladder, with metastases to the liver and lungs.

A PHYSICIAN: Would someone comment on the low chloride?

DR. FRIEDRICH W. KLEMPERER: It was probably due to the vomiting, with consequent loss of chloride.

DR. E. FREDERICK ALSTON: I should like to ask about the significance of the elevated monocyte count. Does this occur with many types of prolonged illness?

DR. CASS: There is a pouring out of monocytes in many types of infection, such as undulant fever and tuberculosis. A single reading of that number, however, does not help me in the diagnosis one way or another, it does, however, suggest tuberculosis.

CLINICAL DIAGNOSIS

Carcinomatosis

DR. CASS'S DIAGNOSIS

Carcinoma of gall bladder, with metastases to liver and lung

ANATOMICAL DIAGNOSES

Acute pulmonary tuberculosis (miliary).

Adenocarcinoma of head of pancreas, with metastases to regional lymph nodes, stomach, liver, abdominal wall and lungs

Tumor thrombi in lungs and liver.

Tuberculosis of bronchial lymph nodes

Pleuritis, acute fibrinous, with effusion

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN The autopsy on this man showed a bizarre picture in the lungs. There was 300 to 400 cc of turbid fluid in each pleural cavity. Both lungs were replaced by yellowish miliary areas of necrosis, some of which were confluent and frankly caseous. Many of the blood vessels were plugged with grayish-white material that looked like tumor thrombi, and this was confirmed microscopically by frozen sections. In the head of the pancreas, just away from the common duct, was a firm granular grayish-white mass, 4 cm in diameter, which was the primary tumor. The liver was riddled with tumor, which had replaced from one third to one half the parenchyma. Here also, as in the lungs, the blood vessels were involved, and the portal vein radicals within the liver were filled with tumor thrombi. Our final sections of the lungs showed that in addition to the carcinoma there was true caseation, and stains for tubercle bacilli showed myriads of organisms. It is almost inconceivable that they were not found in the sputum, since they could be picked out in our sections even under low power. We were unable to find tuberculosis in the sinus tract of the old scar. There was a large tumor nodule beneath the scar, which was a metastasis to the abdominal wall. The tumor proved to be an adenocarcinoma. There were metastases to the regional nodes around the pancreas, some of which had infiltrated the wall of the stomach, so far as we could tell these had not broken through the mucosa, although a number of superficial mucosal vessels containing small bland thrombi were eroded. There was some blood in the stomach, but we could find no evidence of tumor. I imagine that the pressure of the metastatic nodules on the vessels had caused the thrombosis and the subsequent erosion.

CASE 31372

PRESENTATION OF CASE

A seventy-six-year-old widower was admitted to the hospital because of urinary frequency and nocturia.

During the previous six months, overflow dribbling had progressed to spontaneous and uncontrollable voiding, and during the two days before entry he was able to void only a few drops at a time.

There had been no pain, hematuria or previous acute retention.

He had had no venereal disease and no other serious illness, except for typhoid fever about four years before entry.

Physical examination revealed a well developed, well nourished man who appeared well and in moderately severe distress after catheterization. The teeth were in poor repair, and there had been many extractions. The lungs were clear and resonant, with normal breath sounds. The heart was not enlarged. The rate and rhythm were normal, and no murmurs were heard. Examination of the abdomen was negative, except that the liver edge was approximately two fingerbreadths below the right costal margin. A rectal examination revealed an enlarged prostate. The median sulcus was present, and the right lobe felt smooth, soft and about two times the normal size. The left lobe was considerably more prominent than the right, measuring approximately 5 by 3.5 cm, and was quite firm and rubbery. A tense, somewhat fluctuant 1-cm mass was palpated on the lateral aspect of the left lobe. The extremities were negative.

The temperature was 100.5°F, the pulse 80, and the respirations 20. The blood pressure was 140 systolic, 75 diastolic.

Examination of the blood showed a white-cell count of 7000 and a hemoglobin of 75 per cent. The serum protein was 5.3 gm per 100 cc, the acid phosphatase 1.4 units, and the alkaline phosphatase 1.6 units. The nonprotein nitrogen was 34 mg per 100 cc, and the phosphorus 2.4 mg. A blood Hinton test was negative. A catheter specimen of urine was grossly bloody, with a specific gravity of 1.024, and gave a +++ test for albumin. Urine cultures showed *Staphylococcus aureus*, and three consecutive blood cultures yielded *Staph aureus*, all the blood-culture strains were coagulase positive. The organism was found to be penicillin sensitive.

On the second hospital day the patient was cystoscoped. The mucosa was red and edematous. The median and both lateral lobes of the prostate were large and projected into the bladder. The testes were normal. The right vas deferens was slightly thicker than the left, and the globus minor of the right epididymis was swollen, tense and extremely tender. On the third day penicillin therapy was begun, and on the fourth day a suprapubic cystostomy was performed. The temperature, which had been spiking daily to 103°F, returned to normal, the pulse, which had been between 90 and 110, became normal on the fifth day, and the respiratory rate, which had risen to 45 on the third day, returned to 20. The white-cell count rose to 13,400, and the hemoglobin to 85. On the sixth day the nonprotein nitrogen was 60 mg per 100 cc. From the fourth to the ninth day the patient appeared much better and progressed favorably in preparation for a prostatectomy.

During the forenoon of the ninth day he had a sudden chill. The rectal temperature rose to 103.5°F but returned to normal in four hours. The pulse rate was elevated to 110, and the respirations rose to 40. That evening there was slight edema of the ankles. There was moderate dyspnea, and moist crackling rales were heard at both bases. There was no pleuritic pain or signs of consolidation. A loud rough systolic murmur lasted throughout systole, it was heard over the entire precordium but was loudest over the apex. A precordial thrill was felt. X-ray examination on the following morning showed indistinct heart borders due to considerably increased density that extended throughout both lung fields, radiating from the hilar areas into the lungs, this was most marked in the lower lung fields. The density appeared to follow the vascular markings. A small amount of fluid was present in the pleural sinuses. No evidence of infarcts was seen.

On the ninth day the serum nonprotein nitrogen was 42 mg per 100 cc, and the protein 5.3 gm. On the tenth day digitalization was begun. Late that afternoon the patient complained of a vague chest pain. In the evening he experienced sudden distress. He became more dyspneic, orthopneic and cyanotic. He insisted on sitting on the edge of the bed and had a sensation of impending doom. The peripheral pulse was extremely weak, and the skin cool and clammy. The pain in the chest radiated down both arms, and the dyspnea became rapidly severer. The chest was full of loud moist rales, and the heart sounds were distant and irregular. Within thirty minutes of the onset of the distress he expired.

DIFFERENTIAL DIAGNOSIS

DR. PAUL D. WHITE: The urinary difficulties indicate prostatic obstruction. I am not able to relate the typhoid fever to the present story.

This man apparently had a normal heart at the time of entry into the hospital, so far as one can tell from the physical examination. The liver edge was approximately two fingerbreadths below the costal margin, but that was probably due to a low position rather than to enlargement. The prostate was firm and rubbery, apparently not so hard as would be the case in cancer. The fluctuant mass suggests an abscess, of course. The urinary findings seem to be in keeping with prostatic enlargement and infection. The acid phosphatase is within normal range, but that does not rule out cancer of the prostate. Only an increased acid phosphatase would suggest cancer and that is not the case here.

Were any blood cultures taken after penicillin therapy was begun?

DR. BENJAMIN CASTLEMAN: The last blood culture, taken on the fourth hospital day, was positive.

DR. WHITE: And penicillin was given on the third day and continued thereafter. I note that a chill occurred despite the penicillin. How much was given?

DR. CASTLEMAN: Ninety-six thousand units a day.
DR. WHITE: In divided doses, not by drip? That is an important point.

DR. CASTLEMAN: He was given 12,000 units every three hours.

DR. WHITE: I wonder why he had an elevation of the nonprotein nitrogen. Perhaps it was due to renal involvement. The clinical appearance was in keeping with the drop in temperature, pulse and respirations, despite the elevated white-cell count.

This patient, who previously had shown no murmurs or thrill, abruptly developed an unusual cardiac murmur and thrill. I wonder how loud the murmur was. We have had a successful experience in the last year or two, largely owing to close contact with Dr. Samuel A. Levine when re-examining Army cases, with the classification of heart murmurs from Grades 1 to 6. This murmur might have been the type that one can hear with the stethoscope actually off the chest, that is, Grade 5 or 6. It was at any rate a significant murmur.

Are the x-ray films here?

DR. C. HALE: All the pulmonary vascular markings are prominent, and there is also a diffuse haziness.

DR. WHITE: There are no areas suggesting infarction or consolidation?

DR. HALE: I do not see any.

DR. WHITE: The heart is not particularly enlarged. The aorta looks all right for a man of seventy-six.

The nonprotein nitrogen came down terminally, and therefore the patient did not die of uremia. Digitalis was begun the day after the acute complication arose. On the basis of the x-ray findings, it was evidently thought that digitalis was needed. The patient had pain for the first time on the tenth day. The acute illness on the ninth day was not accompanied by pain, — at least there is no statement about it, — but there were dyspnea, a chill and edema of the ankles and lungs. Where was the distress that he suffered on the evening of the tenth day, which was evidently much severer?

DR. CASTLEMAN: Chest pain is all that is recorded.

DR. WHITE: A sense of impending doom is not a reliable symptom in patients who have heart trouble. Nervous persons with simple paroxysmal tachycardia may have a sense of impending doom, whereas people actually dying usually have no such sense. Still, the symptom may be significant here, for he was extremely sick and we may judge by inference that the pain or distress was severe.

In review there are several things that seem clear. Whether there was a prostatic tumor, I do not know, I doubt it. The prostatic infection, possibly retrograde to the bladder and kidneys, was present to start with, and following that came a *Staph aureus* septicemia, which in turn was followed by acute heart failure.

The episode on the ninth hospital day was at-

tended by what sounds strongly suggestive of mitral regurgitation of an unusual nature, probably the result of rupture of a mitral valve cusp or chorda tendinea, secondary to acute bacterial endocarditis. Such a thing could have happened in the course of a week or two, the endocarditis having been silent for a while. Endocarditis due to *Staph aureus* infection is, as a rule, extremely severe and rapid in its course. Other causes of such a murmur with thrill seem less likely. Dilatation of the left ventricle, without structural change, under the stress of illness of any sort may give a murmur, but it is not so pronounced as the one that was found here.

Perforation of the ventricular septum from infection might have occurred, but one would expect that the murmur and thrill would have been nearer the sternum than they were. A rapidly developing aortic stenosis, with large vegetations, should also be mentioned as a possibility but not a probability. Metastatic carcinoma involving the heart is less likely than infection. Complicating septic infarcts of the lungs must be considered, but the electrocardiographic findings do not favor an acute cardiac strain (cor pulmonale) from that source. Thus, bacterial endocarditis, with rupture of a valve cusp or chorda, best explains what happened on the ninth day.

On the tenth day something else happened that precipitated death. This sounds like an acute coronary occlusion, which caused death in half an hour. He had severe chest pain radiating down both arms, with collapse. Pulmonary embolism is unlikely. Coronary atherosclerosis is the most frequent cause of coronary occlusion, but it is more intriguing, of course, to try to fit the picture into one piece. Hence I suggest the possibility, or indeed the probability, of acute coronary embolism due to vegetations on either the mitral or aortic valve. Dissection of the wall of an infected aorta and rupture of the heart wall itself from abscess, with cardiac tamponade, should be mentioned as diagnostic possibilities but they are not likely.

I will stand on the diagnoses of prostatic abscess, *Staph aureus* septicemia, acute heart failure secondary to acute bacterial endocarditis with rupture of the mitral valve or one of its chordae and, finally, acute coronary embolism.

DR CASTLEMAN Dr Smith, you saw this man, would you like to comment on the urinary infection?

DR G GILBERT SMITH The only thing that occurs to me is that he might have had an abscess in the left lobe of the prostate.

DR CASTLEMAN Dr Segall, have you anything to add?

DR HAROLD SEGALL One interesting possibility is that the murmur might have occurred as a result of infection, or infarction, of the myocardium with involvement of the papillary muscle and rupture there. Cardiac rupture frequently starts at the

base of the papillary muscle. In the course of twenty-four hours extension proceeds from the base of the papillary muscle until it reaches the pericardium, this sometimes happens in half an hour.

DR WHITE But he had no pain.

DR SEGALL In old people it may start silently, and the first thing you know the heart has ruptured.

CLINICAL DIAGNOSES

Benign prostatic hypertrophy
Coronary thrombosis

DR WHITE'S DIAGNOSES

Prostatic abscess
Septicemia (*Staphylococcus aureus*)
Acute bacterial endocarditis (*Staph aureus*)
Ruptured cusp or chorda tendinea of mitral valve
Acute heart failure
Terminal acute coronary embolism

ANATOMICAL DIAGNOSES

Acute bacterial endocarditis, with mycotic aneurysm of aortic valve and rupture of commissure between right and left posterior cusps
Adenocarcinoma of prostate
Pylonephritis, mild left kidney
Abscess of epididymis, right

PATHOLOGICAL DISCUSSION

DR CASTLEMAN At the commissure between the right and left posterior aortic cusps was an ulcerated granular thrombosed vegetation that had produced a rupture of both cusps (Fig 1). This ulceration had extended through the commissure as a small mycotic aneurysm, 1 cm in diameter, this had involved the myocardium of the right wall but had not perforated through the endocardium. Perhaps if the patient had lived a few days longer it might have perforated. Each of these cusps had a frayed edge, so that there must have been free regurgitation.

DR WHITE Was the mitral valve all right?

DR CASTLEMAN Yes.

DR WHITE The murmur must have been diastolic, not systolic. The record fooled me.

DR CASTLEMAN There was no involvement of the coronary arteries, unless perhaps a bit of the vegetation on a cusp might have partially covered one of the coronary mouths. It would have had to extend into the right coronary orifice, and at the time of autopsy this was free of disease.

DR WHITE How do you explain the final episode?

DR CASTLEMAN There is only one way that I can think of. Perhaps one cusp frayed on one day and the other on another day.

DR WHITE But there must have been a diastolic murmur, with a diastolic thrill. The examiner obviously timed the murmur wrongly.*

dominant diastolic murmur, owing to flapping of these torn cusps in regurgitation. Do you not agree, Dr Segall?



FIGURE 1

DR SEGALL That could happen if the rate was rapid.

DR WHITE If there was free aortic regurgitation without aortic stenosis there must have been a pre-

DR SEGALL Yes.

DR CASTLEMAN There was no real stenosis.

The remainder of the heart was negative. The prostate was enlarged and quite hard. Microscopically it proved to be an adenocarcinoma. There was an abscess in the right epididymis, and mild pyelonephritis on the left.

*Examination of the record revealed no checkup of the timing of this murmur by internists on the hospital staff. Rupture of an aortic cusp always causes a diastolic murmur, whereas rupture of a mitral cusp or chorda causes a systolic murmur.

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SURVEY OF HOSPITAL FACILITIES

THE American people have been told that the United States needs more hospitals, that existing hospitals in many localities need more beds and that large sections of the country are without adequate hospital service. The reports on which these statements are based have been compiled by various organizations, including the American Public Health Association, and although the facts that they present are undoubtedly correct, the conclusions drawn are open to question.

A lack of hospital facilities, where it exists, is linked in almost every instance with a similar lack of medical service—that is, the absence of hospitals deters doctors from practicing in those areas, and

vice versa. There is no use in having hospitals without competent doctors to staff them. The two must be correlated.

When a physician is confronted with a medical problem he first collects his facts, weighs them, makes his diagnosis and then determines the course of treatment. That is just what the people of the United States want to have done regarding the hospital and medical situation in their respective states. Furthermore, they wish to have this done on a local or state basis, because they believe that their respective states are too big to be satisfactorily treated by a single prescription, even though they desire a co-ordinated national plan.

With this in mind and through the efforts of the American Hospital Association, the Commission on Hospital Care was established last year, being supported by grants from the Commonwealth Fund, the W. K. Kellogg Foundation and the National Foundation for Infantile Paralysis. The objectives of this commission are to take a census of the present hospital and public-health facilities in the Nation, to appraise their capacity for service, to establish standards for evaluating physical facilities, organization and management of hospitals, to determine the overall national need for additional facilities and service, to formulate a national, co-ordinated hospital plan and to suggest methods by which that plan can be realized.

National interest in this survey is already widespread. Thirty-five states are in one phase or another of their studies, and surveys are actually in operation in Iowa, Massachusetts, Michigan, Minnesota, New Hampshire, North Dakota and Wisconsin. Each state is urged to carry on its own study, since in this way local interest will be aroused, each state will become aware of its need, and a desire to furnish adequate service will be stimulated. The commission will act as a co-ordinating body and will furnish a standard questionnaire, as well as technical consultants, for the use of all states making the survey. The final job of tabulation will be done by the commission's staff.

In Massachusetts, Governor Tobin has appointed a committee, headed by Dr. Vlado A. Getting, Commissioner of Public Health, to carry on the survey. A budget has been submitted and will probably be

approved by the Legislature. Certain hospitals have been asked to fill out the standard questionnaire, to gain experience before submitting it to all hospitals.

The efforts of the Commission on Hospital Care, operating on a voluntary basis in true democratic fashion and supported by private funds, bid fair to be supplemented by the passage of a bill (S 191) now before Congress, which would amend the Public Service Act "to authorize grants to states for surveying their hospitals and public-health centers and for planning construction of additional facilities, and to authorize grants to assist in such construction." If passed, the bill would immediately provide \$5,000,000 to assist state surveys and would allocate \$100,000,000 available on June 30, 1946, for the construction of public and other nonprofit hospitals. These two sums could be appropriated each succeeding fiscal year for the same purposes, as determined by Congress. The Surgeon General of the United States Public Health Service would be authorized to make such regulations as are necessary to administer the bill. He would consult with the Federal Advisory Council, consisting of himself, as chairman *ex officio*, and eight members appointed by the Social Security Administrator. States applying for assistance would be required to designate a single state agency as the sole means for carrying out such purposes, provide a state advisory council, meet standards prescribed by the Surgeon General and approved by the Federal Advisory Council and agree to make reports as requested by the Surgeon General. If these requirements are complied with, allotments both for surveys and for construction would be based on the respective state population and financial need, ranging from 25 to 75 per cent of expenditures. Incidentally, essentially the same provisions are included in the Wagner-Murray Bill (S 1050).

The present situation is that state surveys of hospital and public-health facilities are being encouraged and aided by the foundation-supported Commission on Hospital Care. They may possibly be financially aided by the federal government. In any event, knowledge of hospital needs and what is to be done about them should be materially advanced.

THE EPIDEMIC OUTLOOK IN EUROPE

DISEASE and pestilence have always been known to flourish during large wars, to follow in their wake and to add to their ravages. Fresh in the minds of many of us are memories of the great pandemic of influenza that occurred near the end of World War I, of the great toll taken by the epidemic of typhus fever that spread through the Balkans during and after the war and of the other widespread epidemics in eastern and southern Europe that followed it. Although tremendous strides have been made in the prevention of disease in the American armed forces and in those of some of our allies, the outlook for serious epidemics among the European populations in the near future is gloomy. Such is the conclusion arrived at by Knud Stowman* in an analysis recently published by the UNRRA.

Several important factors have led to this pessimistic attitude. When the war came to an end, the civil administrations in most of the countries that are likeliest to be affected were in a fluid state and many of them are apt to be so for some time to come. Even more significant are the mass migrations that gained momentum during the latter phases of the war and still continue. The displaced persons include war prisoners, refugees, slave laborers and those who survived the horrors of the concentration camps. Not only are most of these persons in a condition that makes them highly susceptible to epidemic diseases, but they constitute a serious reservoir of infections, which they will carry back to the native lands to which they are repatriated.

Some of the most dangerous diseases that it is feared may be introduced into previously unaffected areas have already made their appearance to a varying extent in the Mediterranean area, the Near East, North Africa and Dakar. They include plague, smallpox and typhus fever. Yellow fever and cholera have thus far shown no tendency to spread, although an outbreak of the latter disease has been recently reported among the natives in Chungking. On the other hand, the more commonly occurring infectious diseases, such as cerebrospinal meningitis, poliomyelitis, typhoid fever, dysentery, diphtheria and scarlet fever, have all shown a twofold or threefold increase during the war years. This is

*Stowman K. Epidemic outlook in Europe. *Brit. M. J.* 1 742-744 1945

apparently a greater increase than was observed in World War I. Furthermore, the incidences of some of the endemic diseases, such as malaria, syphilis, gonorrhea and tuberculosis, have increased many-fold and at a greater rate than that during the previous war.

Dr. Stowman believes that the absence of any real disasters thus far is due, in part, to the low endemic levels of disease in the years immediately preceding the war. The rapid increases in these diseases during the war, he thinks, serve as an index of what may be expected. The vast destruction of homes, especially in the densely populated cities, together with the great population shifts, when added to the increased prevalence of the common infectious and endemic diseases, makes the outlook for large epidemics in Europe even darker than it was after the last war. The only encouraging feature, which tends to offset those fears somewhat, is the fact that we are now better equipped to prevent and cope with some of these problems. In addition, our knowledge of existing situations is far more complete. Dr. Stowman concludes his analysis with the following pertinent remarks:

On the public health front, World War I lasted not four but more nearly ten years. However, it was gloriously won. Many years of effort in combating infectious diseases have once more been lost so far as Europe is concerned. To make up for backsliding will take several years after the cessation of active hostilities, but the public health profession and services can win their war now as then.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

BARTLEY—John J. Bartley, M.D., of Lawrence, died June 16. He was in his seventy-fourth year.

Dr. Bartley received his degree from Harvard Medical School in 1901. He was Lawrence city physician from 1908 to 1909 and supervisor of school physicians there at the time of his death. He was a member of the Lawrence Medical Society.

His daughter survives.

MEDICOLEGAL ABSTRACT

Medical Schools What standards are to be used in granting approval, adoption of AMA standards. In a recent decision in the New Jersey Supreme Court the action of the New Jersey State Board of Medical Examiners in passing on the application of a graduate of Middlesex University School of Medicine of Massachusetts for licensure was considered.

The graduate, who had been licensed to practice medicine in Massachusetts, sought to compel the

State Board of Medical Examiners to license him to practice in New Jersey by virtue of his license to practice in Massachusetts or, in the alternative, to admit him for examination for license in New Jersey. The application was denied because the applicant had not met the statutory requirement by graduation from a medical school approved by the State Board of Medical Examiners.

The court said in part:

The question to be determined is whether the respondent is justified in classifying Middlesex University School of Medicine as an institution which was not in good standing. It appears that it bases its conclusion in the grading and standing of medical schools on the standard adopted by the Committee of Education of the American Medical Association and makes public the names of the schools which it approves. It is argued by the relator that the action of the respondent in accepting the grading of medical schools by the American Medical Association is without using its own judgment or discretion but constitutes an unlawful delegation of its duty and power. We think not. It is entirely within its discretion, it seems to us, to adopt the standard and grading of an organization of which it has knowledge and confidence. We think it acted within its sound discretion within the meaning of the statute *supra* and was not actuated by arbitrariness or capriciousness. — (*Rothsied v. State Board of Medical Examiners*, 132 N. J. L. 38, 38 Atl. 2nd 444 [1944])

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

PLANS FOR A NEW DENTAL DIVISION

A division of dental health in the Massachusetts Department of Public Health will be created on July 1, 1946, subject to legislative approval of funds for the new division.

It is planned that Lieutenant Colonel Francis B. Carroll, of Waban, will become director of the division. Dr. Carroll is at present with the First Service Command. Prior to that he was with the Department of Public Health as district health officer in the Pittsfield area.

The director and assistant director will be centrally located in Boston and will have technical supervision over dentists and dental hygienists attached to the district offices.

The objectives of the division will be to stimulate more effective dental care of preschool and school children through official and voluntary agencies, to initiate educational projects in dental health in schools, service clubs and other organizations, to assist in special field studies and to inspect dental clinics.

Dr. Carroll graduated from Tufts Dental School and then took postgraduate work in public health at Harvard. After attending medical school at the University of Rochester he engaged in full-time public-health work with the Kellogg Foundation in Michigan, later becoming district health officer with this department. For several years he practiced dentistry in Whitinsville, where he specialized in children's work.

(Notices on page xix)

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THE DIAGNOSIS AND TREATMENT OF CYSTITIS IN WOMEN AND CHILDREN*

HERMAN L. KRETSCHMER, M.D.†

CHICAGO

BY THE term "cystitis" is meant an inflammation of the urinary bladder characterized by frequency of urination, painful urination and pus in the urine. It should be remembered, however, that this clinical triad does not always mean cystitis *per se*, and it is because of this fact that a large number of errors in diagnosis occur.

Although cystitis *per se* in the female — either young or old — is an exceedingly rare condition, the triad of symptoms generally interpreted as indicative of cystitis is extremely frequent in occurrence, with the result that the diagnosis of cystitis is often made but is rarely substantiated. Many patients who present themselves with this symptom-complex are incorrectly diagnosed and incorrectly treated, the serious organic lesions that are the real cause of the condition being overlooked until late in the course of the disease, when conservative surgery becomes impossible owing to the destruction of vital organs.

As a matter of fact, to impress these facts on the minds of students, I frequently make the statement that, in my experience, cystitis in women and children is one of the rarest lesions I encounter, and that for purposes of early diagnosis it should be assumed that cystitis in the female is nonexistent. Furthermore, when symptoms indicative of cystitis are present and no improvement occurs within a reasonable time after medical treatment has been instituted, or when symptoms clear up only to recur at a later period, it becomes imperative that the patient have a complete physical and urologic examination. The most important problem that confronts one when dealing with this type of case is not the administration of this or that drug but the making of an accurate diagnosis to determine the nature and location of the lesion responsible for the symptoms.

The History

The importance of obtaining a good history in each case of so-called "cystitis" cannot be over-

emphasized. An accurate history cannot be obtained hurriedly by an office nurse, and all too often scant attention is given to this. The information obtained generally more than compensates for the time and labor expended.

One must bear in mind that a patient with symptoms of cystitis may be suffering from a lesion in some remote part of the body — that the bladder symptoms may be an expression of a distant disease process. In this category may be placed diseases of the blood, such as pernicious anemia. As an example of a patient belonging to this group, the following case is presented.

A 65-year-old woman, 6 weeks before she was seen by me, had marked frequency of urination and pain on urination and was told there was pus in the urine. A diagnosis of cystitis was made at that time, and treatment consisted of internal medication, bladder irrigations with boric solution and injections of argyrol into the bladder. The patient consulted me for the express purpose of having her bladder washed out.

Examination of the urine was negative. The physical examination showed the knee jerks to be greatly exaggerated, with clonic reactions. Romberg's sign was positive, and the patient walked with some unsteadiness.

The diagnosis, based on the blood examination, was pernicious anemia with secondary degenerative changes in the cord.

Symptoms may be erroneously ascribed to cystitis when they are in truth due to the presence of a congenital anomaly — a condition that in some cases can be readily ascertained by careful history-taking. The following case illustrates the value of obtaining a painstaking history.

A 27-year-old woman was admitted for the relief of what she had been told was cystitis. She stated that she was unable to hold her urine, lost urine between urinations and had been wet all her life. For the relief of her complaints she consulted many doctors and received various forms of treatment, without relief. The treatment included urethral dilatation, applications of silver nitrate to the urethra, instillations and irrigations of the bladder and, finally, dilatation of the bladder.

A careful consideration of one of the patient's statements — namely, that she was unable to hold her urine between urinations — at once suggested the possibility of an ectopic ureter. Examination showed the presence of such a ureter just behind the external urethral orifice.

The onset of symptoms of cystitis after a surgical operation has great significance. Bladder symptoms

*Read at the annual meeting of the New Hampshire Medical Society, Manchester, New Hampshire, May 16, 1944.
†President, American Medical Association.

following an operation are often attributed to cystitis, treatment is instituted without relief, and the patient begins a pilgrimage from one doctor to another. Fortunate she is if the correct diagnosis is eventually established. The patient's statement that the symptoms of the so-called "cystitis" were absent before the operation should at once direct the doctor's attention to the possibility that the operation was a factor in the bladder disturbance.

A history of cystitis given by a patient who has spent part of her life in a sanatorium for tuberculosis, by one who has had repeated attacks of pleurisy or by one with a record of repeated tapings for pleural effusions must at once arouse suspicion that one is dealing with a case of renal tuberculosis with a secondary tuberculous cystitis. A thorough clinical investigation should be made in all cases before beginning local treatment.

In cases in which the patient gives a history of recurring attacks of cystitis, one's suspicion should at once be aroused that some underlying factor is responsible for the recurring attacks, and it is of paramount importance to determine just what that factor is. Not until it has been determined should treatment be instituted. In a certain number of these cases, the recurring cystitis can be traced to a pyelitis or to an infected hydronephrosis.

In some cases of colon-bacillus infection of the urinary tract, with symptoms of cystitis, it may be possible to obtain a history of disturbance in the intestinal tract. As a matter of fact, it is surprising how frequently constipation or cathartic colitis is the causative factor, hence, the importance of directing attention to the intestinal tract before instituting urologic treatment is self-evident.

Physical Examination

The examination should first be directed to the patient as a whole. Although tabes dorsalis is rare in women, the presence of an Argyll-Robertson pupil, absent knee jerks and the presence of Romberg's sign are strong indications that the cystitis is one of the manifestations of locomotor ataxia.

Scars in the neck, the aftermath of suppurating cervical adenitis, evidence of active or healed tuberculosis of the lungs and the presence of an ankylosed joint or scars over bones, the result of long-standing suppuration, must be given very careful consideration in the interpretation of every case of so-called "cystitis." Nor must it be forgotten that other general disease processes are often associated with frequency of urination. It is not unusual to find during the course of the physical examination that the patient suffers from cardiorenal vascular disease, as a result of which there is frequency of urination both during the day and night. In this group of patients, if the urine is free of pus and sterile on culture, the relation between the underlying disease and the cystitis is perfectly obvious. On the other hand if the urine, although grossly clear, shows a

few pus cells and the culture reveals colon bacilli, great care and study are needed to arrive at the proper conclusion.

After the physical examination follows the local examination. This should include a careful examination of the external urethral orifice and Skene's glands. The urethra should be palpated and the strippings examined for pus. A catheterized specimen of bladder urine should be obtained.

With the bladder empty, one should proceed with an examination of the internal genitalia. Vaginal discharge, so often present, should be carefully examined for the presence of *Trichomonas vaginalis*, which is occasionally found in women who are being or have been treated for cystitis. The urine should also be examined for this organism. Next in order is an examination of the cervix and of cervical discharge, if present. Finally, a pelvic examination should be done. It is surprising how often in this group of cases disease is found in the uterus, tubes or ovaries.

One must be careful, however, not to jump at a wrong conclusion and attribute the so-called "cystitis" to pressure from an enlarged fibroid, for it should be borne in mind that a patient may have two lesions, either of which may be responsible for the condition. Double lesions are of relatively frequent occurrence, for example, I saw a patient afflicted with a fibroid and an elusive ulcer and another with a fibroid and renal tuberculosis. Here, as in any other branch of medicine, great care must be exercised in the evaluation of the physical examination.

Lesions in and about the anus and rectum are often the cause of so-called "cystitis." This possibility must be considered in every case before a diagnosis is made.

Lesions of the bowel, such as diverticulitis with peridiverticulitis, may produce bladder symptoms. Here again, only too often the diagnosis is erroneously made.

Examination of Urine

Having obtained a catheterized specimen of bladder urine before the pelvic examination is made, one should proceed to a careful urine examination. When pus has been found in a voided specimen of a woman or girl, nothing other than the examination of a catheterized specimen should satisfy the physician.

If the specimen so obtained is negative and a tentative diagnosis of cystitis has been made, it is imperative that the examination be repeated several times. With symptoms of cystitis present, the urinary examination should determine the presence of albumin, blood (by chemical and microscopic examination), pus cells, red cells, casts and crystals. The urinary sediment should be examined with a methylene blue stain and a gram stain for the presence of bacteria. Finally, no examination of the

sediment is complete without an examination for tubercle bacilli. A part of the catheterized specimen, at the time it is obtained, should be sent to the laboratory for culture.

At this point in the examination of the patient, an appraisal of the mode of procedure should be made. This, I wish to emphasize is to be interpreted as a consideration of the order in which the next steps are to be performed — not as a means of avoiding them. These steps must be carefully carried out in this group of cases in order to make an accurate diagnosis and to determine whether one is dealing with a true case of cystitis or with a case of so-called "cystitis."

Röntgenographic Examination

The x-ray examination may precede or follow the cystoscopic examination. A flat plate of the urinary tract should be made. In a good many cases this is negative, on the other hand, the presence of a shadow in the juxtavesical portion of the ureter compatible with stone, calcifications in the renal area due to stone or calcifications due to renal tuberculosis are extremely informative.

Whether an intravenous pyelogram should be made at this time depends on the history and the results of the examination up to this point. If it is done before the cystoscopic examination, information of great value may be obtained. It is to be remembered that errors in interpretation are frequent and often costly and have led to wrong conclusions. For example, failure of the kidney pelvis to visualize does not necessarily mean congenital absence of the kidney, nor does it mean that the kidney has been destroyed by disease.

Cystoscopic Examination and Ureteral Catheterization

The presence or absence of cystitis must rest on the result of the cystoscopic examination. If this is negative, it is reasonably certain that the patient who is referred with a diagnosis of cystitis does not have it and further study to determine the cause of the symptoms is in order.

Because cystitis in women and children is rare, it is imperative that no patient be treated for this condition for any length of time without a cystoscopic examination. Nevertheless, one sees many patients who have been treated from one year's end to another without a cystoscopic examination's having been made. Should this examination show the presence of an abnormality in the bladder, such as a stone, foreign body, tumor or ulcer, the appropriate treatment can be started at once.

If on cystoscopic examination the bladder is negative, as happens in a large number of cases, the upper urinary tract must be investigated by means of ureteral catheterization. In a large number of cases the primary lesion is found in the kidney. Among the various lesions of the kidney that may

be overlooked for a long time because of the presence of symptoms of cystitis is tuberculosis.

It is a well-recognized fact that in cases of renal tuberculosis frequency of urination is often the first symptom of which the patient complains. Frequency of urination may be due to the presence of tuberculous pyelitis, in which case the cystoscopic examination is negative. When the patient is finally subjected to a careful urologic examination, extensive tuberculosis of the bladder may be found and the bladder may be contracted to such a degree that even after the kidney has been removed and the tuberculosis of the bladder healed, the frequency of urination continues because of the limited bladder capacity. Drugs and bladder irrigations give no relief from the bladder symptoms, in fact, the condition is often made worse by bladder irrigations. When the correct diagnosis has finally been made, such extensive changes have taken place in the bladder that a complete return to normal bladder function is no longer possible.

After the ureters have been catheterized and a specimen of urine taken for a leukocyte count, gram stains, routine and tubercle-bacilli cultures and guinea-pig inoculations and a phenolsulfonephthalein test has been made, a set of retrograde pyelograms may be taken. Whether this should be done depends in part on whether intravenous pyelograms were made before the cystoscopic examination, as well as on the result of the precystoscopic examinations of the urine for tubercle bacilli and the cystoscopic findings. If tubercle bacilli are found or there is reason to suspect renal tuberculosis, retrograde pyelograms should not be made.

Some of the lesions that must be considered in the differential diagnosis of cystitis are listed in Table 1.

Treatment

Once the diagnosis of the underlying lesion responsible for the symptoms has been made, the treat-

TABLE 1 *Lesions of the Urinary Tract To Be Considered in the Differential Diagnosis of Cystitis*

Urethra	Radium burns
Acute urethritis	Foreign bodies
Chronic urethritis	Cystocele
Stricture	Postoperative distortion
Diverticulum	Ovarian cysts
Skenitis	Ovarian carcinoma
Polyps	Cysts of the parametrium
Benign tumors	Lesions of the gastrointestinal tract
Carcinoma	Fissure
Prolapse	Hemorrhoids
Bladder	Carcinoma of the rectum or colon
Elusive ulcer	Diverticulitis with or without rupture
Tuberculosis	Chronic cholecystitis
Stone	General Disease Processes
Polyps	Nephritis
Trichomonas infestation	Diabetes mellitus
Stone	Tabs dorsalis
Carcinoma	Fernicious anemia with cord changes
Incrusted cystitis	
Perivesical adhesions	

ment is perfectly obvious and needs no detailed discussion. It naturally varies, and is as diversified as is the list of possible causes of cystitis just presented.

During the acute stages and during the first attack of acute cystitis, it is important that the patient have complete rest in bed. The application of heat to the bladder area gives a great deal of relief, and hot applications to the suprapubic area are in order. They may be fortified with hot-water bags, in addition, hot vaginal douches with a weak solution of bicarbonate of soda are provocative of good results. Attention to the bowels should consist of laxative foods or mild drugs. Purging is always contraindicated. During the acute stages sedative drugs may be indicated in the form of tincture of hyoscyamus and potassium bromide. In some such cases rectal suppositories containing belladonna and opium give a great deal of relief.

I do not use local treatment, such as instillations and irrigations, during the acute stages. The patient is made much more comfortable by thorough

alkalinization of the urine, and for this purpose I prescribe potassium citrate of potash and potassium acetate and small doses of bicarbonate of soda. I prefer to have the patient on an alkaline regime for a week or ten days, at which time urinary antiseptics, such as urotropin, are administered. It must be remembered that the urine must be acid during the administration of the urotropin. Most of the cases of so-called "acute cystitis" are self-limited, and on this program the patient makes a complete recovery.

If this program fails to relieve the symptoms, or if the symptoms are relieved but recur, it becomes necessary to determine the underlying pathologic factors responsible for the recurring attacks of cystitis. When these have been found, the treatment becomes self-evident.

GLYCOSURIA AND HYPERGLYCEMIA ASSOCIATED WITH ACUTE MENINGITIS

Report of a Case

CAPT JOHN J. FEDERER, M C, A U S *

BECAUSE of the many articles in the recent literature on various manifestations of meningitis, undoubtedly stimulated by the excellent results of chemotherapy, on the Waterhouse-Friderichsen syndrome, with involvement of the adrenal glands, and on the evidence of abnormal carbohydrate metabolism frequently encountered in lesions of the adrenal glands and the hypothalamus, it is thought worth while to present the following case.

A 22-year-old soldier was admitted to a station hospital on June 30, 1944. The past history disclosed no unusual diseases, except for measles, mumps and pneumonia in childhood. The parents, two sisters and a brother were living and well, and no family history of tuberculosis, diabetes, cancer or mental illness was elicited. The patient had been well until 2 days before admission, when he complained of generalized aches and pains, developed a splitting headache and within 12 hours became mentally confused.

Examination on admission disclosed a well nourished, muscular man who was irrational and violent. Both pupils were dilated, and a distinct sweetish odor on the breath and a marked degree of nuchal rigidity were evident. No ptosis of the lids, squint, nystagmus or facial paralysis was found. Nowhere on the skin or mucous membranes were there any purpuric lesions or petechiae. There was considerable redness and injection of the pharynx, uvula and tonsillar tissue, but no membrane formation.

Expansion of the chest was equal and symmetrical, and both lung fields were clear and resonant. The heart sounds were regular and of good quality, with no murmurs or arrhythmia. The pulse was 84, and the blood pressure 104/74. The abdomen was soft and without masses, tenderness or spasm. The liver edge was at the costal margin, and the spleen was not palpable. Deep tendon reflexes were present, and bilateral Kernig signs were demonstrable, as well as Brudzinski signs. Spinal puncture revealed an extremely cloudy fluid under increased pressure (100 drops a minute) and containing 18,000 cells per cubic millimeter, with 90 per cent polymorphonuclear

leukocytes. No organisms were seen on direct smear, and the sugar level was slightly below normal (30 mg per 100 cc). The red-cell count was 4,650,000 and the hemoglobin was 15.5 gm. The white-cell count was 21,000, with 89 per cent neutrophils, 9 per cent lymphocytes and 2 per cent mononuclear cells. Blood and spinal-fluid cultures were done and were reported to be negative. A catheterized urine specimen showed a +++ test for sugar and a ++ test for acetone. The blood-sugar level was 270 mg per 100 cc. A tentative diagnosis was made of meningitis, probably meningococcal, complicated by diabetes mellitus.

The patient was first given 5 gm. of sodium sulfadiazine in 200 cc of distilled water intravenously and 4 hours later 2 gm., with 2 gm. of sodium bicarbonate, by mouth. He could not be induced to take a second dose by mouth, so the sulfadiazine was given intramuscularly every 4 hours. He also immediately received 15 units of insulin. Six hours later another catheterized urine specimen still showed a +++ test for sugar but not acetone. At that time there was given an infusion of 1000 cc of 5 per cent glucose, covered with 20 units of insulin, and an additional 10 units of insulin was given later because of the persistent glycosuria.

Within 18 hours after admission, the patient began to become rational. The blood-sugar level dropped to 117 mg and remained between 97 and 116 mg. Within 72 hours the urine became sugar-free without any further insulin and general improvement was evident. At no time was it possible to demonstrate any organism, either by direct smear or from cultures. Within 12 hours after admission the blood sulfadiazine concentration (Marshall method) was 8 mg per 100 cc, and it was maintained at 12 mg for the next 5 days. On the 6th day, the patient complained of a sharp pain radiating from the left renal area down to the bladder. Since numerous sulfadiazine crystals and red cells were noted in the urinary sediment, alkalization was intensified, and the drug was stopped for 24 hours. No further trouble was experienced from this source. The blood chloride was 417 mg per 100 cc. The blood pressure gradually rose to a more or less constant reading (124/70). A glucose-tolerance test, using 100 gm of glucose, on the 7th hospital day gave the following blood-sugar levels: fasting, 110 mg per 100 cc, $\frac{1}{2}$ hour, 142 mg, 1 hour, 152 mg, and 2 hours, 112 mg. In a repeat test on the 14th day, the corresponding figures were 102, 140, 150 and 100 mg, and in another on the 25th day, they were 104, 144, 152 and 106 mg.

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Convalescence was characterized only by a profuse herpes simplex about the upper lip and nose. On discharge 27 days after admission the patient was symptom-free and had no apparent sequelae. The blood-sugar level was 104 mg per 100 cc., and the urine was sugar-free.

DISCUSSION

In a series of 50 consecutive cases of meningitis, excluding those with meningococcemia but without signs of meningeal irritation, this case alone presented the complications of glycosuria, acetoneuria and hyperglycemia. In the light of the recent literature, the question arises whether this transient pseudodiabetic condition was caused by some adrenal imbalance or hypothalamic lesion, with interference of the carbohydrate metabolism.

Duncan, Semans and Howard* reported a case of abnormal carbohydrate metabolism with hyperglycemia and hypertension in a patient with an adrenal tumor (pheochromocytoma) who was treated over a period of years in the Diabetic Clinic of Johns Hopkins Hospital. On removal of the tumor, all evidence of diabetes disappeared. It is well known that the adrenal glands are the sites of hemorrhage in the frequently fatal cases of the Waterhouse-Friderichsen syndrome. This patient had never had any signs or symptoms of hyperglycemia prior to his infection, and had no history of diabetes. If he had had a subclinical diabetes stirred into activity by the overwhelming infection, it is likely that the condition would not have disappeared when the meningitis was arrested. Subsequent glucose-tolerance tests have shown no abnormal levels. The blood-chloride level was also normal. At no time did the patient present any signs of a fulminating Waterhouse-Friderichsen syndrome, and if the disturbance was not hemorrhagic, this carbohydrate imbalance is difficult to explain. A toxic depression of the adrenal function should have been accompanied by other signs, but it is most unlikely that this would have been favorably influenced by chemotherapy alone. It is also hardly likely that any pancreatic disease would

have been so short lived, for injured islands are notoriously slow in healing.

One other mechanism for the production of hyperglycemia must be considered, that described by Claude Bernard in 1855. He punctured the floor of the fourth ventricle in an anesthetized animal and observed that this procedure produced a prolonged glycosuria. Donnoffer and Macleod found that injury to the pons or the medulla is necessary for the production of hyperglycemia following decerebration. The fact that lesions in the hypothalamus may cause glycosuria has been appreciated for some time. Aschner, in 1912, reported serious disturbance of the carbohydrate metabolism following lesions in this body. Other workers have shown that stimulation of the posterior hypothalamic nuclei produces a hyperglycemia through a disturbance of the sympathetic nervous system. Therefore, a transient lesion in this portion of the brain must also be admitted as a possible cause of the complication described in this case.

SUMMARY

A case of acute meningitis is presented in which there were hyperglycemia, acetoneuria and glycosuria. A satisfactory explanation for these complications remains a matter of conjecture.

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CLINICAL NOTE

A ONE-PIECE MUNRO TIDAL-DRAINAGE APPARATUS

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THE purpose of this report is to illustrate a Munro tidal-drainage apparatus in use at the Springfield Hospital. This hospital is one of 280

tients requiring tidal drainage falls to the lot of interns, with supervision by members of the visiting staff. In view of these circumstances it seemed that a simple apparatus that could be maintained in an assembled state would allow relatively inexperienced interns to avail themselves more readily of this useful technic in patients with cord bladder, incontinence and so forth or with urinary infections in which benefit would be derived by constant irrigation with antiseptic solutions. Instead of being assembled from odds and ends, — a condition that still prevails in some large clinics, — this apparatus

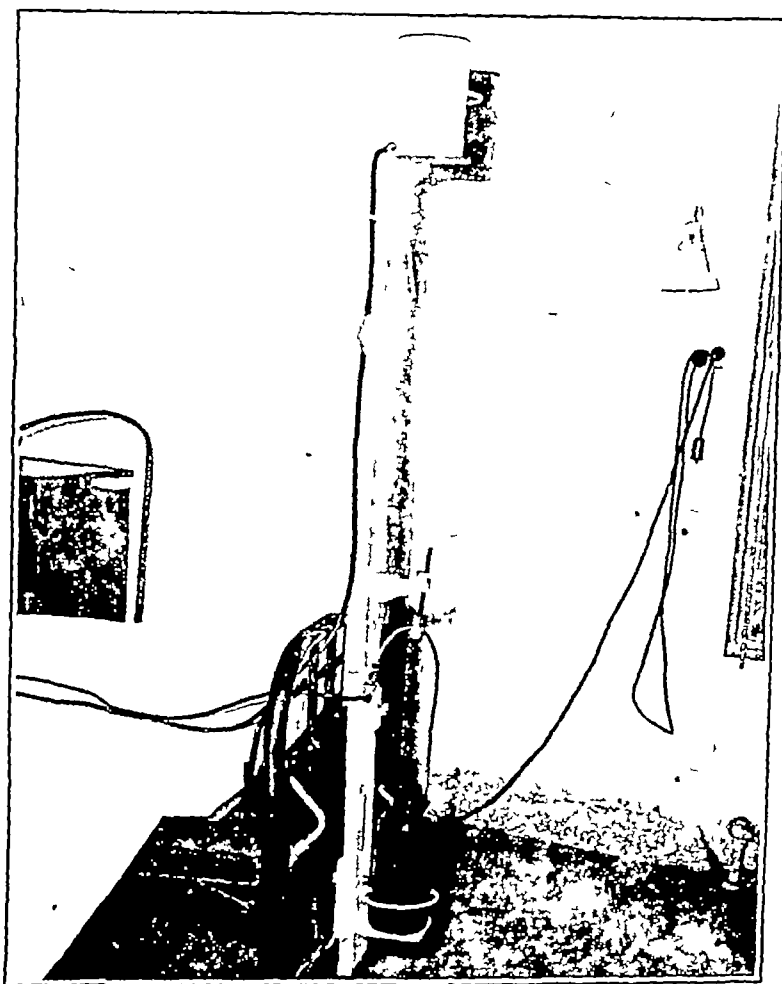


FIGURE 1 Tidal-Drainage Apparatus

The frame is made of steel. A fixed platform supports the can containing the irrigating fluid (a graduated glass container is preferable but was unattainable). The two glass tubes are clamped to an upright measuring stick, which can be raised or lowered in a slot in the frame, being held in any one place by a clamp. The upper end of one of these tubes is turned down at an angle, to permit an overflow during cystometrography. The holder for the outlet tube is removable and can be attached through any of several holes in the frame, to permit overflow at the desired point on the scale. This projecting part acts to protect the glass tubing in handling and transporting the apparatus. The platform holding the overflow bottle is adjustable.

beds, is nonteaching and is without a neurosurgical service. Thus, the responsibility of the care of pa-

(Fig 1) is maintained in such a state that an intern need simply suspend it on the bed, attach the Y tube to the catheter, provide the irrigating fluid and

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regulate the rate of entry of fluid into the bladder and the level at which overflow occurs

This apparatus has been found to increase the frequency with which the average intern avails himself of tidal bladder irrigation. The provision for having the apparatus entirely free of the floor

and firmly fixed to the bed has proved to have practical advantages. It can be moved as one piece and there are no parts to be reassembled or perhaps lost. The apparatus was assembled at the Springfield Trade School, the cost of the materials being \$1 25 121 Chestnut Street

MEDICAL PROGRESS

PHYSIOLOGY (Concluded)

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CARDIAC OUTPUT IN MAN

Methods for estimation of cardiac output in man have been reviewed by Hamilton,²² who suggests that standards at present generally acceptable will probably be revised upward in the future. These standards have been established largely through the careful estimation by Grollman²³ of the cardiac output in 50 normal young adults in the basal resting condition and in a large number of other subjects in a wide variety of physiologic and pathologic conditions. The method employed has been the rebreathing of a mixture of acetylene and oxygen for a variable period as long as 23 seconds, with analysis of the content of the bag at two points to give, after correction for volume changes, the relative rates of disappearance of oxygen and acetylene. Knowing the solubility of acetylene in blood, the amount of acetylene absorbed per liter is calculated for the partial pressures prevailing in each experiment, and from the ratio of oxygen disappearance to acetylene disappearance, the amount of oxygen absorbed per liter of blood passing through the lungs can be calculated. The oxygen consumption per minute is divided by this figure, which is the arteriovenous oxygen difference of the Fick calculation, to give the cardiac output. Grollman's average cardiac output at the basal level was 3 87 liters per minute, with extremes of 2 96 and 4 61 liters. The average cardiac index, or output per unit of body surface, came to 2 21 liters per square meter per minute, with extremes of 1 90 and 2 49 liters.

An apparently major source of error in the method is the matter of recirculation of blood. If blood containing acetylene returns to the lungs during the period between samples, the actual volume of acetylene carried away is less than that calculated, and in consequence the arteriovenous oxygen difference is proportionally too large, and the cardiac output too small. When the period of rebreathing is limited to 10 seconds, which presumably marks

the time when recirculation from such short circuits as the coronary vessels begins, considerably higher values are obtained,^{24 25} but there is as yet no adequate study by this technic in a series of normal individuals in the basic state to compare with Grollman's data. The necessity for some upward revision in basal cardiac outputs is indicated by data which show with little doubt that in the basal condition renal blood flow alone may amount to 1 3 liters per minute.²⁶

The problem has recently come much closer to solution with reports by Stead's collaborators²⁶ and by Cournand and his coworkers,²⁷ who have employed the direct Fick principle in males in the basic state. The arteriovenous oxygen difference is estimated by comparison of the oxygen content of arterial blood, obtained by arterial puncture, and of mixed venous blood, obtained from a catheter threaded through an arm vein into the right ventricle. Excluding determinations in subjects with pulse rates of 82 or above, cardiac indices ranging from 2 3 to 4 1 liters per square meter per minute were obtained by Stead's group, with an average of 3 3 liters. The average index of those subjects exhibiting signs of anxiety was 5 5 liters. Cardiac outputs in the entire series ranged from 4 2 to 14 8 liters. The other group reports cardiac indices averaging 3 12 liters per square meter per minute, the average pulse rate being 60. It is probable that more rigid control of the question of anxiety must be demanded before these values can be accepted in place of the much lower standards hitherto established, the procedure not being one that can be faced by any great number of persons with complete equanimity. The adequacy of mixing of venous blood in the right auricle and ventricle must also be established.²⁸ The swing to an ampler figure predicted by Hamilton has, however, begun

REFLEX DYSPNEA

Two recent studies serve to emphasize the continuing search for a satisfactory explanation for

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the dyspnea of heart failure Mills²⁹ has noticed that the sudden release of blood occluded in a limb by a pneumatic cuff produces a transient hyperpnea in the majority of normal subjects. When ether or cyanide is injected into an occluded vein before release of the cuff, the hyperpnea begins approximately 2 seconds before the ether or cyanide is smelt, and 6 to 12 seconds before the second bout of hyperpnea that occurs when the cyanide reaches the carotid sinus. Making allowances for the latency between the arrival of blood containing ether or cyanide in the pulmonary capillaries and the sensation of smell, Mills concluded that the hyperpnea occurred coincidentally with the arrival of blood in the pulmonary capillaries, and suggested that it was due to a reflex from pressoreceptors in the pulmonary vascular bed. Mills calls attention to earlier observations establishing a relation between respiratory rate and venous pressure, in which intravenous infusions of blood or saline solution, or raising and lowering the limbs in congestive failure, or perfusion of the pulmonary circulation at an increased rate, produced hyperpnea.³⁰ This hyperpnea fails to occur, or is at least almost completely abolished, following section of the vagus nerves, and its occurrence has been attributed to stimulation of receptors in the pulmonary vascular tree or, possibly, in the bronchial system.^{31, 32}

In the other study, that by Altschule, Iglauer and Zamcheck,^{33, 34} observations on cardiorespiratory interrelations were continued. They studied 4 patients with obstruction of the superior vena cava who showed minute respiratory volumes ranging from 7.72 to 13.3 liters, with an average of 9.99 liters. Alveolar carbon dioxide values at the time of obstruction ranged from 4.01 to 5.1 per cent, with an average of 4.58 per cent. After improvement, following irradiation of the occluding tumor or spontaneously, the ventilation rate fell to from 5.86 to 7.2 liters per minute, whereas alveolar carbon dioxide values rose to from 5.18 to 5.55 per cent. The authors are inclined to ascribe the hyperpnea in these cases to stasis in the respiratory center.

In both the experiments of Mills and the cases of Altschule et al, another possibility exists that has not adequately been ruled out, namely, that the hyperpnea in both cases is due to a reflex initiated by increased pressure in the great veins and right auricle. This appears to have been suggested first by Harrison and his coworkers³⁵ from analogy with the Bainbridge reflex. These workers inflated balloons inserted into the superior vena cava and produced hyperpnea, which was abolished by bilateral vagotomy. It is reasonable to suppose that if the hyperpnea in this instance were the result of central stasis, it would have been uninfluenced by vagotomy. The experiment has recently been repeated and confirmed by Megibow, Katz and Feinstein,³⁶ who have added a further refine-

ment in technic by employing an ingenious umbrella-like expander by which the vessel can be stretched without obstruction to blood flow. When this instrument is employed in place of the balloon, which occludes as well as expands, hyperpnea may be produced with equal facility. Although these observations do not rule out the possibility that pulmonary congestion and medullary stasis operate to produce the hyperpnea in congestive heart failure, they direct attention to another factor that must be considered. The degree to which any one of these three factors may be responsible, however, remains to be determined.

NEGATIVE PRESSURES FROM CILIARY ACTION

The experiments of Hilding³⁷⁻³⁹ throw new light on the problem of the pressure changes that occur in the sinuses and in the lungs when the ostium or a bronchiole becomes plugged with mucus. According to the conventional view, the pressure falls as the oxygen trapped within the sealed-off cavity is absorbed by the blood circulating through the lining of the sinus or in the capillaries of the alveoli. For this reason it is often considered inadvisable to permit a patient to leave the operating room after being ventilated with a high concentration of oxygen without first inducing deep breathing with a gas mixture having a more normal oxygen content, with a view to increasing the nitrogen content of the alveolar air and thus diminishing the possibility of complete absorption of the gas in the alveoli and consequent atelectasis if a bronchus or bronchiole becomes blocked. Without denying the possibility that this process does take place, Hilding has shown that significant pressure changes may be produced by ciliary action. Experimenting first with the excised trachea of the hen, Hilding found that when the tube was completely obstructed by a plug of mucus the plug was moved along by ciliary action and, acting like a moving piston, could produce negative pressures behind the plug equivalent to from 4 to 40 mm. of water, and could create a positive pressure ahead of the plug as high as 30 mm. In the sinuses of the dog, negative pressures as low as 66 mm. could be produced by obstructing the ostium by several cubic centimeters of mucus collected from the trachea. The experiment succeeded equally well after decapitation, when all circulation within the walls of the sinus had stopped, without impairment of the efficiency of the ciliary mechanism for some considerable time.

RESUSCITATION

Comroe and Dripps⁴⁰ call attention to the growing importance of resuscitation, which they attribute to the great numbers of persons who are exposed to the risk of drowning through the hazards of war, the increasing number of patients who face the danger of respiratory arrest and circulatory failure through the growing employment of intravenous

barbiturate anesthesia and the introduction of new methods of resuscitation, which compel a thorough review of the efficacy of methods heretofore in vogue. Appropriately, therefore, Fisher⁴¹ reviews the problem in the valuable compilation *Medical Physics*.

The aims of resuscitation are twofold, according to Hemingway and Neil.⁴² In the first place artificial respiration attempts to maintain an adequate pulmonary ventilation, primarily by passive exchange of air and eventually through the revivification of the respiratory center and the resumption of spontaneous respiratory movements. In the second place resuscitation should restore the transportation of blood gases to and from the lungs. The latter phase is essentially directed toward the restoration of cardiovascular efficiency. Its importance is emphasized by Thompson and Birnbaum⁴³ in a paper on asphyxial resuscitation. They call attention to the existence of four stages in the development of asphyxia from tracheal obstruction: the phase of initial apnea, when the breath is held and blood pressure mounts, the phase of dyspnea, when vigorous breathing motions occur and the blood pressure continues to rise, the phase of terminal apnea, with falling blood pressure, and cardiac arrest. If the obstruction is removed before the middle of the third phase, spontaneous recovery is possible, but if asphyxia is carried beyond this point resuscitation is required. During this period, and until cardiac arrest takes place, rhythmic inflation and deflation of the lungs with nitrogen brings about a marked and prolonged rise in blood pressure, during which respiratory movements may be resumed, so that if oxygen is readmitted, recovery occurs without artificial respiration. The phenomenon does not occur if both vagus nerves are sectioned, which suggests that the cardiovascular response is due to afferent stimulation from the lungs, apparently from stimulation of the Hering-Breuer and other afferent nerves by the rhythmic expansion and deflation of the lungs. Denervation of the carotid sinuses and bodies reduces but does not abolish the response. It is therefore apparent that re-establishment of blood pressure and circulation in the medulla plays an important part in the resumption of respiration, and that methods of resuscitation cannot be judged solely by the minute volume of respiration that can be maintained by their use.

The criteria for judging methods of artificial respiration must also include the rapidity with which the method can be placed in operation. This is important in light of observations that the chances of reviving a person after primary respiratory failure are 100 per cent if respiration has just ceased, 97 per cent if respiration has stopped one minute, 92 per cent if arrested for two minutes, 75 per cent for three minutes, 50 per cent for four minutes, and 25 per cent for five minutes.⁴⁰ Methods embodying this requirement are simple mouth-to-mouth insufflation, respiration by means of a hand bellows,

pressure on the rebreathing bag, intratracheal insufflation or the use of a commercial respirator in an operating room where the proper apparatus is available and, finally, manual resuscitation by the Schaefer or Silvester method. There is the greatest danger in failing to apply simple manual measures while awaiting the arrival of mechanical devices.

The Eve method⁴⁴⁻⁴⁶ of resuscitation deserves an important place among the manual methods, employing as it does apparatus that can be improvised rapidly while resuscitation is progressing with the Schaefer or Silvester method. This procedure, which entails rocking the subject through an angle of 45 to 90° at a rate of ten to fifteen times a second, employs the weight of the abdominal viscera as a piston to move the diaphragm up and down the thorax. Thus it has a theoretical superiority over the Schaefer method, the latter depends for inspiration on the elastic recoil of the chest, which fails progressively in the nearly drowned and may be entirely absent after ten to fifteen minutes. Eve's⁴⁴ own words are worth quoting.

Formerly I regarded the breathing thorax as a concertina-bellows, my present work suggests that it resembles rather a cylinder and piston. In older men the cylinder wall is often rigid and is scarcely used in respiration at rest. Hence in artificial respiration it seems much better to exploit the piston action of the diaphragm rather than to try to compress the rigid walls of the cylinder—leaving the piston flapping passively up or down and thus frustrating much of one's effort to squeeze air in and out of the trachea.

The relative effectiveness of the several technics is not entirely clear. The Schaefer, Silvester and Eve methods all are fairly effective in so far as tidal volume of respiration is concerned,⁴⁰ although the Silvester method appears to be somewhat superior to the Schaefer method in some circumstances,⁴⁷ and the Eve method rather more effective than the other two, to such a degree that rocking at a rate greater than fifteen a minute is interdicted because of the possibility of hyperventilation. Apparently, however, the chief advantage of the Eve rocking method is that cardiac output is improved when it is employed. In experiments on dogs anesthetized with Nembutal to the point at which respiration ceased, cardiac output as measured by the Fick method was approximately 25 per cent greater when the rocking method was employed than when thoracic compression was depended on for respiration (1218 cc per minute with the Eve method as compared with 979 cc with the Schaefer method).⁴² Although the respiratory volumes were rather more markedly augmented (1250 and 950 cc per minute by the rocking method as compared with 620 and 580 cc by the Schaefer method), it is likely that the improvement in cardiac output is a result of improvement in venous return when the body is rocked.

No discussion of resuscitation can avoid the question of the efficacy of mechanical respirators in which alternate negative and positive pressures

are exerted on the respiratory cavity, especially after their vigorous condemnation by Henderson⁴⁸. Certainly it is true that no time should be lost in instituting any method of proved usefulness while preparing for the transfer to a more effective or less tiresome method. The Schaefer method is in many, if not most, circumstances the method of choice,^{41, 45, 49} although the Eve method has been employed successfully in a lifeboat at sea.⁴⁹ Mouth-to-mouth insufflation and pressure on the oxygen bag of the anesthetic apparatus are simple and readily available methods in some circumstances,⁵⁰ and small concertina-bellows may be employed as a modification of the fireside bellows first employed by Vesalius for artificial respiration in animals.⁴¹ Henderson is almost certainly correct in interdicting the use of mechanical respirators—or manual respiration, for that matter—once spontaneous breathing has started.

There is, however, not a little evidence that alternate suction and pressure may be effective in resuscitation. Hemingway and Neil⁴² noted that cardiac output during respiration with a pump (probably intermittent positive pressure) was as effective as the Eve method in maintaining a high cardiac output. Birnbaum and Thompson⁶¹ employed rhythmic alternate negative and positive pressures (equivalent, respectively to 9 and 14 mm of mercury) in producing asphyxial resuscitation and found that the suck-and-blow method employing oxygen was the most effective method of resuscitating anesthetized dogs asphyxiated by obstruction. Coryllos⁵² reports that, after the development of the third stage in asphyxia (apnea with falling blood pressure), manual resuscitation loses its effectiveness because of loss of muscle tone and that forcible insufflation is the only effective measure. No evidence of damage by the method was found in experimental and clinical cases. Ross⁵³ has collected data on 66 cases of successful resuscitation by the alternate sucking and blowing respirator, which include 33 newborn infants, and in no case was evidence of injury noted. Thirty-three cases of successful resuscitation by the Schaefer method are also presented, and there are again no reports of damage by the method. In no case was there revival if more than fifteen minutes intervened between respiratory arrest and the institution of resuscitation.

On the other hand, there is the observation of Holt,⁶⁴ who permitted dogs to breathe spontaneously from spirometers filled with air under positive (18 to 16 mm of mercury) or negative (8 to 16 mm of mercury) pressure. Cardiac output, as measured by the Fick or a modified Stewart method, decreased on the average of 33 per cent with positive pressure and changed extremely little with negative pressure. The conditions in these experiments hardly permit one to draw conclusions applicable to artificial respiration. Marcotte et al.⁵⁵ report the

development of extensive subcutaneous emphysema after inflation of the lungs in man with a positive pressure equivalent to 12 mm of mercury. The same observers note the development of emphysema in cats after exposure to positive pressures equivalent to 16 to 20 mm of mercury and in the dog after inflation to a positive pressure of 24 mm or over, a fall in blood pressure was noted after an increase beyond 14 mm. Beecher, Bennett and Bassett⁵⁶ observed a rise in venous pressure, a fall in systolic, diastolic and mean arterial pressures, a decrease in blood flow in the femoral and carotid arteries and in the superior mesenteric veins and a slowing of respiration when anesthetized dogs were exposed to a mean intratracheal positive pressure equivalent to 10 mm of mercury. This alteration in respiratory and circulatory dynamics is without significance in normal animals but may be the cause of death in shocked animals. Rasmussen and Adams⁵⁷ noted that periodic inflation of the lungs with pressures equivalent to 20 to 50 mm of mercury at a rate of 28 per minute lowered blood pressure to the point of cyanosis, and was followed by embolism and hemorrhage in 2 out of 9 dogs.

It is therefore probably justifiable to conclude that, despite possible dangers that have not been unequivocally demonstrated, mechanical respirators of the suck-and-blow type are useful when properly employed in the right circumstances, which would appear to warrant further studies of the procedure.

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NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-FOURTH ANNIVERSARY

House of Delegates, May 14 and 15, 1945 (Concluded)

The report of the Committee on Medical Preparedness was then presented by Dr. Smith

Report of the Committee on Medical Preparedness

During the past year only a few additional physicians have been commissioned in the armed forces. With the return of medically discharged officers to civilian practice, other physicians will be declared available and urged to apply for commissions in the Navy, which urgently needs doctors.

As this report is being written, Selective Service occupational deferment affidavits are being obtained on all essential physicians under thirty-eight years of age.

The number of inquiries regarding practice in New Hampshire from doctors in service is gratifying. The number of men and women establishing practice in our state at the present time, however, is small—far from sufficient to counteract the loss from death and disability. As a result, the situation in some localities is becoming quite acute. There can be little or no relief for the present, since discharges from the Army to care for the civilian population are difficult to obtain.

DEERING G. SMITH, *Chairman*
EZRA A. JONES
CARLETON R. METCALF

Dr. Robinson said that the Committee on Officers' Reports wished to congratulate the members of the Committee on Medical Preparedness for their present and past accomplishments in this exceedingly difficult and delicate task. It was hoped, by world circumstance, that their further activities might soon become unnecessary. He moved the acceptance of this portion of the report, and the motion was duly seconded and carried.

The report of the Committee on Mental and Social Hygiene was then presented by Dr. Baker.

Report of the Committee on Mental and Social Hygiene

The agencies in behalf of social and mental hygiene in New Hampshire have changed little since our last report. Their accomplishments, however, have been gravely hampered by want of personnel. The state institution so deficient in staff members that it cannot do its necessary work, can hardly undertake extramural activities. As

mentioned in the last report of this committee, the amount of extramural work undertaken by the staff of the State Hospital should either be recognized and financially supported as an approved activity of that institution or provided for separately as an approved activity disconnected from the institution.

It may be no information to mention the fact that all state institutions have been carrying on as best they can with some loss of efficiency, and some loss of the high standards maintained when more help was available.

The twenty-fourth biennial report of the State Department of Health covers many subjects of social hygiene that for the sake of brevity are not mentioned here.

The nervous system of any human being will break under sufficiently severe and prolonged strain. War subjects thousands to these severe prolonged stresses. Many men are returning with nervous systems as badly injured by such stresses as other parts of the body would be by shrapnel. It is to be regretted that there are not available more physicians with experience and understanding of mental and nervous derangements. The escape from fear and anxiety and the return to normal human conditions and familiar occupation will help many of these men to recover. Many, however, would be greatly benefited by a larger number of physicians wise in the ways of the mind.

B. W. BAKER, *Chairman*
JOHN B. MCKENNA
SIMON STONE

Dr. Robinson said that the Committee on Officers' Reports was confident that it voiced the reaction of the House of Delegates in taking recognition of the excellent character of the service rendered to the State through its people who are mentally ill by those public institutions delegated to their care. He moved the acceptance of this portion of the report. The motion was duly seconded and carried.

Dr. Robinson then spoke as follows:

It is the considered opinion of your committee that the stresses of war on the nervous systems of our people, both military and civilian, will multiply a thousandfold, a problem that, even before this cataclysm, has had no adequate answer in New Hampshire, namely, the proper psychiatric aid to people mentally ill but not insane or feeble-minded.

We suggest that the Committee on Mental and Social

Hygiene be directed to make a proper study of this situation, unless such study has already been made, and formulate a plan that, if it appears practical of accomplishment, is to be considered for approval at some later meeting of the House of Delegates, and that, when and if approved, the Committee on Mental and Social Hygiene, with the help and assistance of the Committee on Public Relations, shall take the necessary steps to vitalize this plan through legislative action

Dr Robinson moved the acceptance of this portion of the report. This motion was duly seconded.

Dr Sycamore asked whether there was any member of the committee present who would speak to the motion. The Secretary requested that Dr Robinson again describe what the combined committee was to do and the study they were to make. Dr Robinson replied as follows:

It is merely a suggestion that the Committee on Mental and Social Hygiene be directed by the House of Delegates to make a proper study of this situation, that is, the need for outpatient psychiatric care in New Hampshire, this being subject to the provision whether such study has already been made. I do not know about that. Then it is to formulate a plan covering what activities the psychiatrists consider to be necessary. It is to present this plan at a future meeting of the House of Delegates—perhaps next year. If it is approved, the committee, with the help and assistance of the Committee on Public Relations, will take the necessary steps to get the necessary money, I suppose through appropriation through the Legislature, to activate the plan.

Dr Metcalf said that he considered this a "large order." The Society had encountered a similar situation in connection with the draft. All the men rejected for the draft, he explained, are sent back for a checkup in six months. They all have to come to Concord, because the only psychiatrists in the State are at the State Hospital. He did not know just how an outpatient checkup was to be conducted in Portsmouth or Berlin on these cases, or how the Legislature would feel about it. He was, however, perfectly willing to do his part in recommending it, if it was essential.

Dr Robinson replied as follows:

Dr Baker in a telephone conversation expressed his feeling that there was a definite need for more psychiatric coverage, as an outpatient service. He said that, although the need was there and although an attempt had sometimes been made to answer it by employing an extra staff man when one was available, the State Hospital still had no authority to do so, and he believed that the scope should be so broadened that some adequate plan could reach, perhaps, the bare necessities of the State.

I am confident, as a practitioner of medicine, that there is a crying need for someone to whom patients may be sent for more help than we can give them within our own unspecialized knowledge.

I have a letter from Dr Baker, which reads as follows:

It has always been most difficult for the best informed on a special sized topic to present the knowledge to the majority for the benefit of the majority. This has been done on many occasions through the process of begging. Religious missionary work is based on begging; we call it voluntary contribution. Red Cross work, so essential is contributed to in the same way. For years New Hampshire has supported clinics and instructed on tuberculosis through the process of a certain kind of seal. For a good many years Massachusetts which has many state institutions has maintained an extra staff officer at each institution for extramural work. This work consists largely in the holding of clinics together with the public schools for the identification of psychoneurotics and mentally deficient children.

In New Hampshire, clinics of a similar nature have been started and carried on by the Community Council, of Nashua, the Children's Aid and Protective Society of Manchester, and the Board of Public Welfare in co-operation with the State Hospital. Our Board of Educa-

tion maintains no psychiatrist. The social worker from this institution frequently tests for school superintendents on request.

Since these clinics are educational and desirable, the sustenance cannot be based on seals of any kind, and it seems to me that their existence should be requested by the New Hampshire Medical Society and some source of support be recommended. This support should be in the form of a biannual appropriation for this purpose. There would be needed heated and convenient rooms, a social worker to obtain a school and family history and the economic status, and a psychologist and a psychiatrist to examine patients and, with the aid of the evidence obtained by the social worker, to advise as to the best form of procedure.

Provision for these rooms and the personnel must come from somewhere; small under staffed state institutions cannot supply it. So far the State Hospital has paid and maintained Dr Philbrook for this purpose.

I think it would be well for the House of Delegates to give a little thought to the desirability of these mental hygiene clinics and to the fact that they have no substantial recognized basis of support. Conceivably the maintenance of clinics of this kind could be provided for by specific appropriations or the Legislature could provide additional funds for this purpose to be expended by the Board of Health or the Department of Public Welfare. My main purpose, however, is to remind the delegates of the value of these clinics, and that they are being maintained without a substantial economic basis. If they are desirable, an expression of the approval by the New Hampshire Medical Society would be instructive to the public and helpful to the clinics.

It was on the basis of this letter and on the basis of the report of the committee that the Committee on Officers' Reports felt that the proper procedure was for the committee to produce a concrete plan of what they wanted—not a rambling one, but something specific. Then, if it met with approval, the committee could go ahead with it.

The Speaker said that the gist of Dr Baker's letter seemed to be that he would like to have the House of Delegates go on record as supporting some plan and pushing the onus of supplying it back to the Committee on Mental and Social Hygiene. Dr Robinson agreed.

Dr Clough said that anyone practicing medicine or surgery realized the benefit of this plan. At the present time, in the case of patients questionably psychoneurotic, the only place to get a consultation outside of Hanover was Concord and Laconia. It was very difficult, he asserted, to convince a patient who did not feel anything particularly wrong with him to go to the State Hospital for consultation. He believed that if this plan went through, a separate building should be established, with proper waiting rooms to take care of these people.

The motion was then put to vote and was carried.

The report of the Committee on Tuberculosis was then presented by Dr Kerr.

Report of the Committee on Tuberculosis

The mortality and morbidity of tuberculosis is steadily being reduced among the people of New Hampshire. If the incidence of active cases continues to decline as it has during the past few years, we may look forward to the virtual eradication of human tuberculosis throughout the State in the not too distant future. This prediction, of course, depends on the continuance of an increasingly effective campaign against the disease by the New Hampshire Medical Society, public-health officials and other workers.

The death rate from tuberculosis in New Hampshire during the war years 1941-1943 has been slightly decreased as compared with the three prewar years of 1938-1940. Although statistics for 1944 are not yet available, reports indicate that its death rate will approximate the all-time-low point of 1942. This is remarkable in view of war's unfavorable effects, such as longer hours of labor and increased physical and mental stress.

The Bureau of the Census report for 1943 shows that New Hampshire is among the eleven states throughout the Nation with a death rate from tuberculosis lower than 30 per 100,000 population. States with this death rate in 1943 were Utah, 11.2, Wyoming, 14.3, Nebraska, 16.9,

Iowa, 187, Kansas, 194, Oregon, 219, North Dakota, 227, New Hampshire, 258, Wisconsin, 258, and Minnesota, 279. This record is remarkable in view of the fact that New Hampshire is the second highest industrialized state in the Nation in proportion to its population.

It is estimated that approximately 79,000 chest roentgenograms have been made in the past five years in New Hampshire in programs by the New Hampshire Tuberculosis Association, the State Department of Health and the State Induction Center. These examinations include the x-raying of pupils, teachers and janitors in schools and colleges, surveys on workers in industry and selective service men, and examinations in the chest diagnostic clinics of the New Hampshire Tuberculosis Association. A fairly representative cross section of the population of the State has been examined.

The greatest number of clinically active cases of tuberculosis are referred by physicians to the chest diagnostic clinics. One hundred and eighty-five physicians referred patients with suspicious symptoms and signs to these clinics in 1944. The next largest number of clinically active cases is found among the contacts of the above cases. The third largest number of active cases is among the Selective Service rejectees. It should be mentioned that an exceedingly small number of active cases were found among the pupils, teachers, school janitors and workers in industry.

Despite New Hampshire's low mortality and morbidity from tuberculosis, the tubercle bacillus still remains the greatest cause of death among the communicable diseases. This is because there is no specific curative agent for human tuberculosis as there is for diphtheria, syphilis and other communicable diseases. For treatment of this condition the medical profession must continue to rely on early diagnosis, prolonged rest and the other measures mentioned in last year's report. Even the far advanced cases can be arrested and cured as has been amply proved in the lives of many New Hampshire people. We are watching with interest the careful experimental work being done with promine, diazone and related compounds. According to recent reports the toxicity of these substances still hinders their practical application in human beings.

Since tuberculosis will always remain an infectious and communicable disease, no physician can avoid his responsibility in preventing this disease through the early diagnosis and prompt segregation of tuberculous patients. New Hampshire physicians are to be commended for their fight against the tubercle bacillus thus far. Not only has the mortality rate from tuberculosis been greatly lowered, but recent survey work shows that the incidence of active pulmonary lesions among the apparently well people in New Hampshire has become amazingly low.

The fact remains, however, that tuberculosis is still the master thief of human life and efficiency among the communicable diseases of New Hampshire. The lifting of wartime travel restrictions will expose the population to new sources of infection. The finding of positive tuberculin reactors and calcified primary lesions in school children still points to the presence of active cases in this state. The germ is being beaten throughout the State, yet it still lurks in a few strongholds. Surveys elsewhere show that undiscovered cases may be found among the routine admissions of patients to hospitals and institutions. Your committee therefore recommends that the New Hampshire Medical Society give its wholehearted support to a program for chest x-ray examination of all hospital admissions as a routine procedure. In addition, we urge continued co-operation in chest x-ray examination of all members of tuberculous households and those who have been in close proximity to patients with active pulmonary tuberculosis.

ROBERT B. KERR, Chairman
RICHARD C. BATT
CHARLES H. PARSONS

Dr Robinson expressed his committee's sincere admiration for the results accomplished in New Hampshire from efforts directed toward the eradication of this disease and the care and cure of those afflicted with it. He congratulated the members of this committee for the invaluable service they were rendering the State. He moved the approval

of this portion of the report, and the motion was duly seconded and carried.

Dr Robinson then spoke as follows:

Your committee, subject to further information not now in its possession fails to see the value of taking routine chest x-ray films of all hospital admissions. Conceding that there is strong argument in favor of routine chest x-ray films on all people in certain age groups and on all people with a history of exposure to tuberculosis, it appears to us that there are other more practical approaches to the detection of the unsuspected case. For instance, we wonder if routine tuberculin tests, repeated at regular intervals on all children of school age, with a campaign through education and chest x-ray examination of members of the families of the reactors, would not be less expensive and accomplish more.

He moved the approval of this portion of our report.

Dr Sycamore said that he would hate to see the New Hampshire Medical Society go on record as opposed to routine x-ray examinations in hospitals. He added that there were other conditions besides tuberculosis, physicians were dealing in hospital admissions with sick people, not with a large group of well people. He acknowledged that at the present time there was a shortage of films. Subject to Dr Robinson's approval, he favored amending the motion to read that the routine examination by x-ray at the present time is impracticable.

Dr Robinson replied that the report was subject to information not now in the committee's possession. The committee believed that the routine x-ray examination of people admitted to hospitals was one of the poorest approaches to the problem that could be conceived. He could see no purpose in taking chest x-ray films of a ninety-four-year-old patient with a hypertrophied prostate. He could see the value of routine x-ray examination of the gastrointestinal tracts and of routine kidney x-ray films since they gave a better picture of the patient, but from a practical standpoint he felt that the substance of the report should be approved.

Dr Davis said that the usual allotment of x-ray films had been met by one third, and that it would be humanly impossible to do such a thing at the present time.

The original motion was duly seconded and was carried with two dissenting votes.

Secretary Metcalf then spoke as follows:

The Committee on O P A Assistance has lost two of its members. Dr Parsons and Dr McQuesten resigned, and for several months Dr Barbeau of Manchester, has carried on alone. I saw the head of the O P A recently, and he said that Dr Barbeau had done a fine job but had been overworked. The Committee on Nominations is now confronted with the dilemma that Dr Barbeau has also resigned.

The chief work of the committee was in checking on the use of cream and rationed products by doctors, that is if a doctor applied for an amount of cream for a patient that seemed to be excessive, the O P A wanted to have a consultation with a committee that could say "yes" or "no," and that could decide whether or not the request was a reasonable one.

Dr Robinson moved the abolishment of the Committee on O P A Assistance, and spoke as follows:

I fail to see any particular value that the committee has rendered to the physicians of the State. It has been nothing but an annoyance to me, and I think that this is probably true of a great many of the men. Although there may be some effort at co-operation and although there may be somebody who has the practical approach to the thing, I have failed to see any indication of this.

Not more than a week ago I had a patient come to me who, a year and a half ago, was in the hospital with a severe case of diabetes. She was put on a carefully balanced diet, and as she was not a particularly intelligent person she was given definite instructions to follow the diet in detail. She was given permission and a sufficient number of points to get the food required — until the point values were altered, when she could no longer get the proper amount and kind of proteins. She went to the Ration Board, but they could do nothing about it. She had to get a letter from her physician stating exactly how many more food ration stamps she had to have because of their change in value. I told her that she was on a diet that should be sufficient, that the Ration Board knew what she needed, and that it was up to them to supply her with a sufficient number of stamps. I then got a lengthy questionnaire as to why she needed the extra points.

This type of procedure is simply an incident in a multitude of annoying circumstances. I still do not think, on the basis of the type of co-operation that the O P A shows, that they are worthy of any help from us.

Secretary Metcalf said

Before this committee was appointed the O P A was quite hard-boiled in the matter, and there was a good deal of indignation on the part of doctors because it was turning down cases that the doctors thought were legitimate. So it has worked both ways. Undoubtedly, this committee of doctors has procured extra amounts of food in some cases, where otherwise they would have been turned down flat by the O P A, which is composed of nonmedical men who cannot decide about diets. I think there has been more satisfaction since this committee was appointed than there was before. At any rate, there was a lot of satisfaction until Dr Barbeau resigned.

Dr Robinson still moved the abolishment of the Committee on O P A Assistance. His motion was duly seconded, and on vote of the delegates present, was lost.

Dr Dye moved that the Councilors' reports be not read, because they would be printed later in the *Transactions* of the Society. This motion was duly seconded and carried.

Speaker Tuttle asked whether the county societies had any members they would like to propose for affiliate membership in the Society. Dr Clough moved that Dr Fred A Sprague, of Merrimack County, be made an affiliate member of the Society. This motion was duly seconded and carried. Dr Tower proposed the name of John Butler for affiliate membership in the Society. This motion was duly seconded and carried.

Dr Clough asked whether it would be possible to reconsider the suggestions to be made to the Legislature regarding the establishment of psychiatric clinics. He doubted that another state-controlled clinic of any sort was desired. It might well be better to encourage the location of psychiatrists in different localities of the State where they would be used, away from institutions. Such men could get established in New Hampshire after the war and there would be no need for these clinics. He asked whether the motion could be withdrawn.

Dr Robinson replied that the substance of the recommendation was that whatever plan the Committee on Social and Mental Hygiene proposed should have the full approval of the House of Delegates before any action on it was taken. That should be satisfactory for the present, since the committee could not take any constructive action until the House approved the plan presented. He suggested that the committee survey the situation and propose a plan. He believed that every individual in an activity that was worth while should be given the opportunity to present his side concretely. He was not in favor of the invasion of state-controlled medicine in the private field, but thought that the committee should be given the opportunity to propose a plan, it then being a matter of consideration and judgment by the House of Delegates as to whether it met with its approval. Dr Clough said that this explanation was satisfactory.

The report of the Committee on Communications and Memorials was then presented by Dr Davis.

Report of the Committee on Communications and Memorials

Two weeks ago, I got the announcement that I was appointed chairman of this committee, and three days ago, I received some communications from Dr Metcalf. Most of these have been taken up here tonight, and I do not think they need any further reference before the House of Delegates. However, I shall have a meeting with my committee and report back on one communication regarding the care of infants, this matter was taken up last year and discussed thoroughly in the House of Delegates. It is the same old thing over again, but I shall report on that matter, after I have a committee meeting.

STILLMAN G DAVIS, Chairman

The Speaker asked whether Dr Davis had in mind the medical and surgical care of soldiers' wives. The latter replied, "Yes."

Dr Chamberlain said that the first year the Society did not accept the care of infants, it being thought by the powers that be that maternity care could be had without infant care. As to infant care, the reason why it was being brought up again was that the Children's Bureau in Washington had inquired whether the Society was not going to include all the benefits that are available under the plan. He thought that New Hampshire was the only state that had not accepted these benefits. After one year with maternity care alone, the infant part of the plan was accepted. There are several things that were not accepted on the recommendation of the Committee on Maternal and Infant Welfare, these matters were taken up in the House of Delegates.

Dr Dye asked what benefits had not been accepted. Dr Chamberlain replied, "The medical and surgical care of infants." Under the plan, he added, if a woman got pneumonia during the prenatal period, her physician could receive a fee for her care, besides the obstetric care. The same thing was true in surgery. The requirement in the

care of medical conditions, other than holding a license to practice in New Hampshire, was that the physician must be a graduate of an approved school of medicine. In surgical care, the surgeon must either be a member of the American Board of Surgery, or be eligible to it, to be an assistant to the consultant, a man must have had one year's residency in his specialty in surgery and be in the practice of surgery for one or two years. He said that the only reason for the matter's being brought up was that the Bureau had been asking all year whether the Society could include medical and surgical infant care in the plan. It might say that the entire plan must be accepted or rejected. He therefore sought the reaction of the delegates, because the present plan held until July 1, and an answer would be wanted then.

In reply to questioning, Dr. Dye said that the same qualifications held true for both medical and surgical infant care up to one year of age, and that circumcision was not included in surgical care. Complete maternal care included the care of the newborn for two weeks, with no charge to the patient.

Dr. Dye said that the only hitch was that infant care had already been accepted. Dr. Chamberlain replied that it included no major surgery.

Dr. Clough said that last year, when the plan was approved, there were probably no more than four or five members of the House of Delegates who practiced obstetrics. He quoted an article in *Medical Economics* as stressing that this program, without question, as already planned, was to be continued indefinitely. He therefore believed that either the whole plan should be rejected or an opinion should be obtained from those practicing obstetrics. He did not think that it was fair for those engaged in specialties, such as nose-and-throat work or just surgery or special forms of it, to be voting on this plan when it did not affect them at all, and when they did not understand it.

Dr. Dye asked the Speaker about the reaction of the New England Obstetrical and Gynecological Society to the plan. The latter replied that not much of anything was said at the last meeting about the proposition, but that in private conversation the members expressed the opinion that the plan was all right in certain cases, but that the fee was not high enough. Most of them appeared to favor some method, provided that the fees were put a little higher, and that infant care was not included for quite so long. It seemed to be asking a good deal for a physician to take care of a baby for a year, after taking care of the mother at a reduced rate, carrying her through pregnancy and delivery. He asked how many of those present practiced obstetrics, and over half the delegates present raised their hands.

Dr. Clough said that the physicians who deliver

servicemen's wives should be the only ones to vote on this question.

Dr. Robinson then spoke as follows:

I think that during the continuation of the war emergency there is a great deal of reason why some plan of benefit to the wife of the private soldier or seaman should be continued. There are a great many features of this particular plan that are disagreeable. I do not like the idea of anyone's telling us in New Hampshire who is qualified to do what. I think that is a province that belongs to the Society and the physicians themselves.

My own feeling about it is that we should go on record as against accepting provisions of qualification beyond the provisions that we require in our own state for the performance of the same service, and beyond that, express our willingness to co-operate.

Dr. Clough asked whether the members would consider giving these people free care, the patients themselves paying the hospital.

Speaker Tuttle spoke as follows:

It seems to me that the only mothers who are allowed to have this care at the present time are those of the first four or lower pay-grades of servicemen. When they are in higher grades than that, they have to pay for their own care, and also for their hospital care. In the cases that I have taken care of, I received \$55.00 up to November 1 and \$50.00 since then, whereas previously all I ever got from the same family was what I call "25 cents for return of the birth bounty." So it has been of considerable benefit to me.

These people could not possibly afford to pay any more than what you are getting, and it seems to me that the plan should be accepted while the servicemen are away. They know that their wives are going to be well taken care of. When they come back, it is up to us to see whether or not this stops. But until that time I am heartily in favor of keeping this thing going.

Dr. Lawrence then spoke as follows:

I think that you are acting wisely in proceeding in the manner that you are. Certainly it would be a great mistake, so far as public support of our profession is concerned, if we refused to take care of these women, the wives of servicemen who are sacrificing their lives for us.

Now, in regard to the manner in which the Bureau is conducting itself, that is open to a great deal of criticism, and when the time comes for the servicemen to be out of the picture, something definite can be done. You have indicated one or two instances in which, by declaration, the Bureau tells you what must be done. Well, it has gone much farther than that. It has issued a circular in which it is stated under what conditions the Bureau will approve a state plan, which is the reverse of what was planned. It was originally intended that each state should submit a plan under which it could work, and that this would be approved by the Bureau. It was suggested that there might be some reason for not approving every detail, but now they have reversed that, the circular stating the conditions under which you may co-operate.

I think that, so far as fears of state medicine are concerned, this is even worse than the Wagner Bill. But again, let me say that I think it would be unwise to refuse to do things now, because it would be thoroughly misunderstood. I think that you should co-operate.

Dr. Clough said that the whole program was a failure in some cities because the wives had to go on a ward, and in large hospitals like the Boston Lying-in, in going on a ward, they were taken care of by the interns or the students. This meant that the physicians in the city were not contributing a single thing toward the program. It was persons like himself, up in the country, who had to take

care of these patients and spend twenty-four hours or more with them. Yet he would much prefer keeping his self-respect and taking care of them for nothing to signing up with this outfit. He moved to reconsider each year this program on maternity and infancy care, at least until the war was over. He added that so many men were going to continue in the armed forces that the profession would be taking care of the servicemen's wives forever, unless the line was drawn somewhere. This motion was duly seconded and carried.

Dr. Dye called attention to Article XIII of the Constitution and By-laws, reading as follows:

The House of Delegates may amend any article of this constitution by a two-thirds vote of the delegates registered at that annual session, provided that such amendment shall have been presented in open meeting at the previous annual session, and that it shall have been sent officially to each component county society at least two months before the session at which final action is to be taken.

In this connection, he said, the change of "affiliate" to "life" in Section 3 of Article IV could not be voted on at this meeting. Under the Constitution, the proposal should be brought out in the open meeting the following day. Two months before the next annual meeting, it should be sent to the component county medical societies. At the next House of Delegates meeting, the change might be voted on.

With reference to the by-laws, he and Dr. Jones moved that Section 3 of Chapter XI of the by-laws be amended to read as follows:

When the total sum of the Benevolence Fund reaches \$10,000, the House of Delegates may increase or decrease the yearly allotment from the dues of each member to the fund and shall also decide whether the income from the general fund shall continue as a source of revenue to the Benevolence Fund, except that at the time of any regular meeting of the House of Delegates, the yearly allotment may be abolished, increased or reduced for a period of one year only, by unanimous vote of the members of the assembly.

He moved that the matter be laid on the table until the next meeting. He also moved that the General Fund return to the Benevolence Fund the amount that it failed to receive under the regular provisions of the by-laws last year, stating that last year, under this section, the fund did not reach \$10,000. Since it had not reached \$10,000, the House of Delegates was not privileged to abolish the contribution of 50 cents per member from the General Fund to the Benevolence Fund, the previous year it had been \$1.00.

Dr. Robinson asked what the by-laws say with reference to the amount of contribution that is to be made to the Benevolence Fund. Dr. Dye quoted, "The Secretary-Treasurer shall apportion each year to the Benevolence Fund, fifty cents from the dues of each member."

Dr. Robinson then moved that the Benevolence Fund refund the amount of 50 cents a year for every year the General Fund paid \$1.00.

Dr. Dye said that an attempt was being made to adjust an illegal action of the House of Delegates. The first illegal action, he said, was to raise the contribution from 50 cents to \$1.00.

Secretary Metcalf stated that this was done for one year. In other words, 50 cents too much was paid in 1943 and 50 cents too little in 1944, so that so far as the fund was concerned, it was on an even keel.

Dr. Kingsford asked how if the contribution was dropped the Benevolence Fund was to get any more money by contributions from members.

Dr. Dye answered by saying that at the moment the income from the Society dues was down because many of the members were in the armed services. This amendment, he said, gave the House of Delegates the privilege of voting each year on how much of the dues should be taken for the Benevolence Fund. When the membership returned to its normal status, it could be voted to increase the income.

Dr. Dye's motion to lay the matter on the table was duly seconded and carried.

Dr. Robinson then moved to amend Dr. Dye's second motion to the effect that the Benevolence Fund should return to the General Fund the amount it received over and above what it should have received under the by-laws. Dr. Dye accepted the amendment, and this motion was duly seconded and carried.

The report of the New Hampshire Physician Service was then presented by Dr. Sycamore.

Report of the New Hampshire Physician Service

In compliance with the vote of the House of Delegates last year, the New Hampshire Physician Service was duly incorporated in May, 1944, and the first policies were issued as of August 1, 1944. In the first eight months of operation, 15,000 subscribers have been enrolled — a remarkably rapid rate of growth. Approximately 80 per cent of the subscribers have surgical coverage only, the remaining 20 per cent having the combined surgical and medical policy.

Financially our experience has been equally favorable. A total of \$13,240.00 was subscribed by members of the New Hampshire Medical Society and interested friends as a working capital. Of this amount \$4,331.44 was expended to cover the organizational expenses and the operating deficit of the first five months. Beginning with January of this year, income overtook expenses, and a balance has been accumulating that is now sufficient to cover an adequate reserve for unreported services and an additional reserve sufficient to repay the original capital investment. It is to be remembered, however, that substantial reserves will be necessary to meet the added load of the second year of operation owing to the automatic termination of the first-year restrictions governing the coverage of pre-existing conditions and obstetric care.

The striking success of our program so far is a tribute to the ability and efficiency of our executive-secretary, Mr. R. S. Spaulding, particularly since he has been handicapped, like everyone else these days, by a shortage of personnel both in the office and in the field.

This success is an indication also that our program is meeting a definite need and that the people of New Hampshire are eager to secure the protection it affords. This, then, as a corollary, imposes on us as the physicians of New Hampshire the obligation of giving our full and enthusiastic support to the Blue Shield, and of making every

effort to secure 100 per cent co-operation by the members of our society

L K SYCAMORE, *President*

Dr Robinson for the Committee on Officers' Reports suggested that this report, both interesting and concise, required no additional comment except to urge again the members of the Society to give this experiment their unstinted co-operation until it will have proved itself, to the practice of medicine, as either a benefit or a detriment. He moved the acceptance of this portion of his committee's report, and the motion was duly seconded and carried.

Dr Sycamore said that it was a provision of the Enabling Act that the majority of the Board of Directors be approved by the House of Delegates. He therefore moved the approval of the following Board of Directors of the New Hampshire Physician Service:

L. K. Sycamore
C. A. Rollins
James Ross
Harry L. Additon
Frank J. Sulloway
Rt. Rev. Mgr J. S. Buckley
O. E. Cain
Francis J. C. Dube
Fred Fernald

James W. Jameson
James M. Langley
Joseph E. LaRoche
Carleton R. Metcalf
J. J. Morin
Ray W. Pert
Richard W. Robinson
James H. Winter

This motion was duly seconded and carried.

A motion to adjourn was duly seconded and carried, whereupon the first meeting was adjourned at 10 50 p. m.

* * *

The House of Delegates reconvened at the Hotel Carpenter, Manchester, on May 15, 1945, at 8 30 a. m., with Speaker Ralph W. Tuttle, of Wolfeboro, presiding.

The following members answered the roll call:

The President, *ex-officio*
The Secretary-Treasurer, *ex-officio*
Richard W. Robinson, Laconia
Francis J. C. Dube, Center Ossipee
W. J. Paul Dye, Wolfeboro
Walter H. Lacey, Keene
Walter F. Taylor, Keene
Arthur B. Sharples, Groveton
Ralph N. Jones, Whitefield
Leslie K. Sycamore, Hanover
Israel A. Dinerman, Canaan
George F. Dwinell, Manchester
Sullivan G. Davis, Nashua
Robert E. Biron, Manchester
William P. Clough, Jr., New London
Harry B. Carpenter, Portsmouth
George G. McGregor, Durham
William R. Latchaw, Somersworth
Francis Nolin (alternate for Donald C. Moriarty, Sullivan County)
B. Read Lewin, Claremont

Dr Dye moved that the House of Delegates approve the proposed change in the Constitution. This would not, he explained, be a final vote. It was to be read before the general meeting that afternoon. Two months prior to the next meeting, each county society would consider the proposal, and then it would be voted on at the next annual meeting. The changes were that Article IV, Section 1, of the Constitution be amended to read, "This

Society shall consist of members, life members, and honorary members" and that Article IV, Section 3, be amended to read, "Life members shall be those members whose dues are remitted." This motion was duly seconded and carried.

Dr Dye then moved that Chapter 1, Section 5, of the by-laws be amended to read as follows:

Any physician who has been a member of this Society for a continuous term of fifteen years and is either not less than sixty-five years of age, or totally disabled, on the request of his county society may be made a life member on a majority vote of the House of Delegates. Life members shall have the same rights and privileges as other members of the Society but shall not be required to pay dues.

This motion was duly seconded and carried.

Dr Dye then moved that Chapter 3, Section 1, of the by-laws be amended to read as follows:

The general meetings shall include all registered members, life members, honorary members and guests, who shall have equal rights to participate in the proceedings and discussions, and, except guests and honorary members to vote on pending questions. Each general meeting shall be presided over by the president, or in his absence, or disability, or by his request, by the vice-president. Before it, at such time and place as may have been arranged, shall be delivered the annual address of the president and the annual orations, and the entire discussions relating to scientific medicine.

This motion was duly seconded and carried.

Dr Dye then moved that Chapter XI, Section 3 of the by-laws be amended to read as follows:

When the total sum of the Benevolence Fund reaches \$10,000, the House of Delegates may increase or decrease the yearly allotment from the dues of each member to the fund and shall also decide whether the income from the general fund shall continue as a source of revenue to the Benevolence Fund, except that at the time of any regular meeting of the House of Delegates, the yearly allotment may be abolished, increased or reduced for a period of one year only, by unanimous vote of the members of the assembly.

This motion was duly seconded and carried.

Dr Clark, reporting for the Committee on Nominations, proposed three men, president Charles F. Keeley, Claremont, John A. Hunter, Dover, and Richard W. Robinson, Laconia. He said that Dr. Gile had withdrawn, because of illness, from the office of president.

On written ballot, Dr. Robinson was elected president.

Dr. Clark then proposed three men for vice-president: Walter H. Lacey, Keene, Ralph W. Tuttle, Wolfeboro, and George F. Dwinell, Manchester.

On written ballot, Dr. Tuttle was elected vice-president.

Dr. Clark then read the rest of the slate, as follows.

OFFICERS

Councillors for five years

Henry H. Amsden, Merrimack County
Timothy F. Rock, Hillsborough County

Trustee (for three years)

George C. Wilkins, Manchester

- Speaker of House of Delegates* Deering G Smith, Nashua
Vice-Speaker of House of Delegates Leslie K Sycamore, Hanover
Necrologist Henry H Amsden, Concord
Delegate to A M A (1945-1946) Deering G Smith, Nashua
Alternate Delegate to A M A (1945-1946) Emery M Fitch, Claremont

STANDING COMMITTEES

Amendments to Constitution and By-laws

W J Paul Dye, Wolfeboro
 Willard C Montgomery, Epping
 Ralph N Jones, Whitefield

Child Health

Colin C Stewart, Jr, Hanover
 B Read Lewin, Claremont
 Franklin N Rogers, Manchester

Control of Cancer

George C Wilkins, Manchester
 Ralph E Miller, Hanover
 George F Dwinell, Manchester

Maternity and Infancy

Robert O Blood, Concord
 Benjamin P Burpee, Manchester
 Marion Fairfield, Nashua

Medical Economics

Leslie K Sycamore, Hanover
 Richard W Robinson, Laconia
 Francis J C Dube, Center Ossipee

Medical Education and Hospitals

John P Bowler, Hanover
 James W Jameson, Concord
 Samuel M Brooks, Manchester

Medical Preparedness

Deering G Smith, Nashua
 Anthony E Peters, Portsmouth
 Harold I L Loverud, Manchester

Mental and Social Hygiene

Benjamin W Baker, Laconia
 John B McKenna, Hanover
 Simon Stone, Manchester

O P A Assistance

Brockway D Roberts, Durham
 Colin C Stewart, Jr, Hanover
 Simon Stone, Manchester

Public Health

Harris E Powers, Manchester
 Anthony E Peters, Portsmouth
 Alfred L Frechette, Concord

Public Relations

The President
 The Vice-President
 The Secretary-Treasurer
 Robert J Graves, Concord
 Joseph N Friberg, Manchester

Publication

Carleton R Metcalf, Concord
 Raymond H Marcotte, Nashua
 Robert Flanders, Manchester

Scientific Work

Carleton R Metcalf, Concord
 Robert R Rix, Manchester
 Sven Gundersen, Hanover

Tuberculosis

Robert B Kerr, Manchester
 Richard C Batt, Berlin
 Rufus R Little, Glencliff

The Secretary was instructed to cast one ballot for the remainder of officers and committee members, as nominated, this was done, and all were declared duly elected

Dr Sycamore then spoke as follows

I have been requested by Charles M Batchelder, chairman of the Loan Committee of the State Banking Association, to present for your consideration a plan proposed by the American Banking Association to their state association groups, known as the Blue Triangle. This is the bankers' plan of arranging loans for the patient who cannot pay the bill by cash and wants time to do it.

Briefly, the doctor has the forms from the bank in his office, and instead of making arrangements for the patient to pay him over any certain period of time, he has the patient sign a note, and the doctor signs it with him, then the bank will discount the note. For example, on a \$100.00 note, the bank pays the doctor \$90.00. The patient then makes his arrangements through the bank. The extra \$10.00 goes to a fee to cover any bad notes signed, and if this amount exceeds at any time 10 per cent of the other standard loans, the doctor can withdraw. The banks are interested in the plan because it gives them a chance to let some of their money out at interest.

From the doctor's point of view, I think the plan has two main advantages. The first is that it takes out of his hands the bother of collection, the second is that the patient is more likely to pay promptly a business institution than he is the doctor. The doctor, of course, is still responsible. He is a co-signer of the note and is therefore responsible if the patient does not pay the bank. Under this arrangement, he is in the same position that he would be if the patient did not pay him, so that he has nothing in particular to lose and has something to gain.

The plan has been approved by the Massachusetts Medical Society and has worked out satisfactorily in Massachusetts. The New Hampshire Bankers' Association would like to have the approval of the House, if it sees fit, so that it can put the program into effect. It would probably be advisable to refer this question to a committee to work with the bankers' committee, to decide on the specific details.

In answer to questions, Dr Sycamore explained that the bank holds 10 per cent of the note in the "kitty" for bad loans, and if the "kitty" is not sufficient, the doctor is responsible for the amount of default. The service charge is about 6 per cent. The bank takes the usual steps to make the patient pay after he signs the note. If the "kitty" gets large, anything over 10 per cent may be withdrawn on standing loans.

Dr Dye moved that Dr Sycamore's proposal be accepted, and that it be referred to the Committee on Medical Economics for such co-operation as they saw fit. This motion was duly seconded.

Dr Robinson observed that there was nothing particularly new in this plan, it had been in use in the community for a long time. He saw little advantage in the 10 per cent withholding feature, as proposed, over the usual method of procedure. He thought, however, that the matter should receive consideration by the Committee on Medical Economics.

In answer to a question by Dr Sycamore, the Speaker explained that the committee was to report back the following year.

Dr Robinson asked whether the House of Delegates and the maker of the motion would be willing to accept a further amendment, namely, that the

committee be empowered to investigate and act, if in its judgment this was thought to be advisable

The speaker stated that the House would have to approve it. It seemed to him that the motion covered the whole situation

The Secretary-Treasurer pointed out that if the matter was left thus, nothing would be done until a year later. The question was, Did the House wish to hold the question in abeyance for a year, or to go ahead with it, or to kill it? He added that a year could be saved by deciding the question then

Dr Dye then withdrew his motion, and moved instead that the House of Delegates go on record as approving the principle of note collection in co-operation with the New Hampshire Bankers' Association, and that the Committee on Medical Economics be empowered to act in this connection. This motion was duly seconded and carried

Dr Dinerman proposed a vote of thanks to the Manchester Committee for their efforts in organizing this meeting and for their arrangements of it. This motion was duly seconded and carried

The report of the Committee on Communications and Memorials was then presented by Dr Davis

Report of the Committee on Communications and Memorials

The Committee on Communications and Memorials recommends the continuance of the program that has been in operation in New Hampshire for the past two years, namely, the EMIC program, which provides for the care of the wives and infants of the servicemen in the lower four pay groups. This program was discussed at length in the House last night, and it was voted that it should be brought up for discussion each year. The committee favors the continuation of the program for the coming year

Inquiries have been received in regard to the Association of American Physicians and Surgeons. Information was requested from the American Medical Association. That body was never consulted by the organizers, and there has been no action on the part of the Association of American Physicians and Surgeons, other than an intensive and persistent campaign for membership and the distribution of letters written by the president.

One section of the by-laws that was widely distributed throughout the United States provided that when 75 per cent of the physicians in a community or area had become members, they would not maintain professional relations with physicians who had not become members. This provision of the by-laws was widely criticized in the journals of the state medical associations, county medical bulletins and at least two outstanding newspapers. No information could be given of its present membership

The other communications received by your committee were taken up and referred to the proper committees

Committee on Officers' Reports

Dr Robinson for the Committee on Officers' Reports said that no action was to be taken on the communications. His committee, he added, had made a recommendation regarding the Association of American Physicians and Surgeons in its report that seemed to cover the situation adequately

It was moved that the Society continue with the EMIC program, as it had the previous year. Dr Dye spoke to the motion as follows

The matter of the medical and surgical care of mothers and infants deserves special attention. As Dr Chamberlain said last night, it is probably necessary that we consider this extra provision of the EMIC program. She said that pressure was being exerted on them, in connection with the adding of surgical care to the mother and infant care, and she raised the question what would happen to the regular obstetric care if the whole program was not accepted. It seems to me that we should take some action on this matter instead of merely agreeing to carry on as we did last year

Dr Clough, who spoke at length last night, is to be commended for his idealism, but there is a war on, and there exists this EMIC program for wives and infants in the lower-paid brackets of the armed services. If we do not co-operate with it as long as the war is in effect, we shall lay ourselves open to much criticism. Every newspaper in the country will be saying that this group will not co-operate in the care of the wives and children of these poor boys-fighting in foxholes all over the world. Furthermore, the boys want us to co-operate

It seems a necessary evil that we shall co-operate fully with the EMIC program, at least for the duration of the war. After that we should be against anything like that in medical practice. I should like to amend the motion to include the extra provision regarding surgical and medical care of mothers and infants, as provided for under the program

Dr Metcalf said that he thought that the previous year's agreement included everything except surgical care. The authorities in Washington had laid down rigid rules about surgical care, based on the alleged opinion of a group of prominent surgeons

The requirements, he said, were that no man could do surgery on these wives and children unless he were a diplomate of the American Board of Surgery. He stated that there were only three men in New Hampshire who were so qualified

Dr Dye said that there were about twelve such men

Dr Metcalf said that the feeling last year was that any man who was doing good surgery in a general hospital in New Hampshire was qualified to take out the appendix of a serviceman's wife. If he could not conform to the steamroller from Washington in that respect, that was another thing. As a result, he said, a motion to continue the program would mean that the Society was doing everything that Washington wanted done except surgery, for which the New Hampshire physicians and surgeons were apparently not qualified

Dr Dye agreed with Dr Metcalf. Section b, he pointed out, did not say that a man would necessarily have to be a diplomate, but that he must be eligible for the Board or have had adequate surgical experience and be approved by the State Board of Health to perform surgery. He approved of the principle that in this state a man who is a recognized surgeon among the profession should be granted that privilege by the State Board of Health and so listed. He said he would like to add to his motion that the Society would carry on with the surgical care as well, but that it went on record as holding that all surgeons recognized as such on their own hospital staffs throughout the State should be approved for this service

Dr McGregor said that the program was fairly

satisfactory, and he had heard no complaints about its conduct. He pointed out that if the Society accepted the proposal and had surgery done only by men considered competent, this would involve a committee to decide who was competent and a great deal of ill-feeling among the members. The whole thing seemed to be rather involved. He advocated continuing the present procedure until after the war and then abolishing it.

Dr Dye repeated his motion that the EMIC program be continued. Dr McGregor asked to amend it to the effect that this terminate the discussion until the end of the war.

Dr Dye pointed out that at the previous meeting it had been voted to discuss the matter every year until the war was over.

Dr Robinson then spoke as follows:

This matter seems simple enough. We have expressed ourselves as being perfectly willing to co-operate to the best degree of our ability in this plan, for the sake of the boys in the service. In regard to the motion, none of us apparently like it, and we do not intend to carry on the program any longer than it continues to be a contribution toward the spirit and welfare of these boys that are making such great sacrifices.

Washington or the Department of Labor or whoever is responsible should be notified that we are willing to provide the facilities to handle this care, and we should carry the plan on as of last year, because the same reasons exist now as existed then.

Dr Dye's motion was then duly seconded and carried.

Dr Dube asked whether it would be proper to take up the question of payment to the individual doctor on the old-age assistance cases. It had been brought to his attention by quite a few men that the old-age medical expenses were paid not to the doctor but to the patient, sometimes the doctor got it and half the time he did not. If he did get it, it was usually parceled out to him \$2.00 this month, \$1.50 the next month and so on. A bill of \$25.00 or

\$30.00 might take six months or more to be collected. He also raised the question whether there ought to be a revision of the fees paid on old-age assistance. The fee schedule originally agreed on under Bill 417 was slightly revised several years ago, but it was, he said, still far below the normal fee. Some doctors seemed to think that in these times, with the butcher, the baker and the landlord getting higher fees, doctors ought to have some provision for a different fee schedule.

Secretary Metcalf said that this question had been taken up the previous year by the Committee on Public Relations and that long conferences were held with the Public Welfare Department and the county commissioners. At that time, a fee schedule was drawn up that raised the fees about 25 per cent. He continued:

So far as paying the money to the patient or to the doctor is concerned, Washington is adamant, they say that if it goes directly to the doctor the patient is humiliated, and I believe that it will be absolutely impossible to change the routine. I also believe that having increased the fee schedule about a year ago, it is unlikely that there will be any increase this year.

The only thing I suggest is that the matter be referred again to the Committee on Public Relations. I do not believe that any motion passed here would have the slightest effect on Washington or anybody else, under the circumstances.

Dr Sycamore moved that this matter be referred to the Committee on Public Relations. This motion was duly seconded and carried.

Dr Dye moved that the next annual meeting be held in Manchester. This motion was duly seconded and was carried.

Dr Dye moved that the meeting be adjourned. This motion was duly seconded and carried.

The second and final meeting of the House of Delegates was adjourned at 9:45 a.m.

CARLETON R. METCALF, *Secretary*

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor**

BENJAMIN CASTLEMAN, M D, *Acting Editor*

EDITH E PARRIS, *Assistant Editor*

CASE 31381

PRESENTATION OF CASE

A fifteen-year-old boy was admitted to the hospital complaining of vomiting.

Two years before admission the patient first noted pain in the wrists and ankles following an upper respiratory infection. Precordial pain was also present. He had no nosebleeds but vomited several times. He stayed in bed several weeks and then gradually resumed his usual activities. He remained well until about six months before admission, when he caught a "cold" and developed a nonproductive cough, along with chest pain. Several weeks later he began to have nosebleeds and migratory joint pains, these symptoms persisting for about three months. During that period he noticed marked dyspnea and chest pain on exertion, orthopnea and ankle edema. Frequent headaches also occurred, coming on in the late morning and being most severe over the right eye. He lost about 17 pounds in weight. He occasionally had blurred vision, but no diplopia or dizziness. There was no history of convulsions. A week before admission the patient complained of nausea and since then had vomited once a day, usually in the morning. Soon after arising he usually passed several loose stools. He had epigastric pain and eructations. No joint pains were noticed, and there was no upper respiratory infection. Irregularities in the heart rate were occasionally noted. Episodes of costovertebral-angle tenderness occurred.

Physical examination revealed a well developed and well nourished boy in no acute distress. The skin was warm and moist. The cervical and axillary lymph nodes were palpable. The heart was enlarged 3 cm beyond the left midclavicular line. A harsh diastolic murmur was heard over the aortic area, and a faint systolic murmur along the left sternal border. At the apex a low-pitched, rumbling, diastolic murmur and a blowing systolic murmur were present. Rales were present at both lung bases. The neck veins were slightly distended and pulsated. The liver was palpable two fingerbreadths below the right costal border and was tender. The tendon reflexes were somewhat depressed. Duroziez's mur-

*On leave of absence

mur was heard over the femoral arteries, and "pistol shots" over the antecubital arteries.

The temperature was 97°F, the pulse 100, and the respirations 20. The blood pressure was 140 systolic, 55 diastolic.

Examination of the blood on admission showed a red-cell count of 4,800,000, with 11.4 gm of hemoglobin, and a white-cell count of 4500, with 61 per cent neutrophils, 32 per cent lymphocytes, 2 per cent monocytes, 4 per cent eosinophils and 1 per cent basophils. A week later the red-cell count was 4,600,000, and the white-cell count 10,600. Urinalysis on admission showed an occasional white cell and granular cast. Succeeding specimens were negative. The corrected sedimentation rate on admission was 0.35 mm per minute, rising steadily to 0.80 mm per minute a week before death. Serologic tests for syphilis were negative. The serum chloride was 86 milliequiv per liter. Repeated blood cultures were negative. The stools were negative for occult blood.

Fluoroscopy revealed enlargement of the left ventricle and auricle. The heart pulsation was distinct. The hilar blood vessels were engorged and the vascular markings were increased throughout both lungs. There was no evidence of pleural effusion. An electrocardiogram showed a normal rhythm, at a rate of 100 per minute. The PR interval was 0.16 second, and the PR wave was normal, S₁ was small, with a slight left-axis deviation, Q₁ was small, ST₁ sagging, T₁ diphasic, T₂ upright, ST₂ elevated, T₂ upright, and QRS, M-shaped. The venous pressure six days after admission, following transient clinical improvement, was equivalent to 100 mm of water. The circulation time by the ether method was 6 seconds, and by the calcium levulinate method 20 seconds.

During the patient's hospital course the temperature varied from normal to 104°F. The pulse varied from 80 to 130, being usually about 110. The respirations were 20, rising at times as high as 50. The patient remained dyspneic and orthopneic, and dullness appeared in the lung bases. The pulse later became both alternating and slightly paradoxical. On the fourth hospital day the patient vomited twice and complained of abdominal pain and general discomfort. A week later these symptoms became severer and more persistent. Liver enlargement increased. The patient was treated with complete bed rest, salicylates, digitalis, moderately limited fluids, ammonium chloride, Mercupurine, phenobarbital and a Schemm diet. The patient expired on the nineteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR T DUCKETT JONES: I should like to have the heart murmurs clarified. The description is not clear to me.

DR BENJAMIN CASTLEMAN: I shall read what the cardiologist said.

There is a systolic murmur at the apex, less well heard at the base, and a low-pitched apical rumble, which may actually consist of two diastolic heart sounds. There is also a rather scratchy diastolic murmur of moderate pitch, best heard in the pulmonic area but also heard along the left sternal border. The pulmonic second sound is active.

DR JONES Did he say anything about the diastolic murmur being heard at the aortic area?

DR CASTLEMAN It was best heard in the pulmonic area, but I imagine that it was also heard along the left sternal border.

DR JONES May we see the x-ray films?

DR MILFORD D SCHULZ These films were made two days apart, and there is no great change between the two. There is no evident fluid in the pleural sinuses. The hilar vessels are prominent and the heart is enlarged in all diameters. The aortic knob cannot be seen, and the left upper border is so straight that if the note did not say distinctly that the cardiac pulsations were good, one would wonder if there were not some effusion into the pericardium.

DR JONES But they made a distinct note that the pulsations were good. This is a picture more of left-sided than of right-sided hypertrophy?

DR SCHULZ There certainly is a fair amount of the cardiac shadow to the right of the midline, much more than a person of this age should have.

DR JONES It seems perfectly obvious that this boy had heart disease. The story goes back for at least two years, and one wonders whether he did not have some active process going on in the heart for most of that time. I presume that he was seen by a physician two years before when he was in bed and that if we had records from that physician we could be certain of definite heart disease then. His symptoms were very suggestive of heart failure early in the course of his process. At the time of onset of both illnesses this boy had mild joint symptomatology, which is thoroughly in keeping with rheumatic fever, but may occur in a great many other conditions. Patients with tuberculosis may have joint pains of a mild degree. Patients with disseminated lupus erythematosus have joint symptoms. The pains were never severe. Certainly the experience in this war has been that joint symptomatology is a striking feature of our diagnostic criteria and has to be considered one of the major diagnostic points in rheumatic fever, especially in the presence of evident heart disease, such as there is here. It is perfectly obvious that this boy had free aortic regurgitation. At least he had all the signs and symptoms of it. I cannot conceive of the findings having been anything else unless there was some strange and unusual congenital anomaly, which I should not expect. Progressive aortic disease in young people with rheumatic heart disease is not infrequent.

The boy apparently had a mitral diastolic rumble, and as you know, well over 90 per cent of patients with rheumatic heart disease have some evidence of

mitral valvulitis at autopsy. The aortic murmur, however, seemed to be predominant over the diastolic murmur heard in the mitral region, and I suppose the question should be raised whether the apical diastolic murmur was an Austin Flint type of murmur. I should say that there is no way of being certain of this. Where there is rheumatic heart disease it is impossible to be certain of an Austin Flint murmur, because the rheumatic process itself causes mitral valvulitis in such a high percentage of cases.

I do not believe that it is likely, but it is possible, that the findings here were on a basis other than rheumatic fever. We know well that pericarditis causes considerable enlargement of the heart in all its diameters at times, and in some cases of pericarditis one may find all the murmurs that go along with rheumatic heart disease and which we usually consider to be evidence of valvulitis. So I think that we must differentiate here between pericarditis of undetermined etiology, possibly tuberculous, and rheumatic fever. I should think that the chief features are strongly in favor of rheumatic fever for the following reasons. He had obvious aortic disease, which, so far as I know, clinically does not occur even in greatly enlarged hearts due to pericarditis. His age is all right for rheumatic fever. The duration of the process is rather typical of some of the severe and progressive cases of rheumatic fever, and his chronic illness with severe heart failure is also quite characteristic of rheumatic fever. Perhaps he had more chronic left-sided heart failure than most young rheumatic fever patients have. He apparently had a great deal of therapy. As you doubtless know most of the young rheumatic fever patients have more right-sided failure than they do the left-sided or mixed types. In fact those who die with a fulminating acute occurrence of rheumatic fever usually do so with right-sided failure that comes on quickly, and their end comes rapidly. This boy, however, had cardiac enlargement, and it is probable that the left-sided and mixed pattern is accounted for by the left ventricular disease, which was a combination of infection and of the mechanical aortic defect.

Against pericardial disease of nonrheumatic origin there are a good many features. The majority of patients who develop Pick's disease (polyserositis, constrictive pericarditis, mediastinopericarditis) have some evidence of cardiac tamponade, such as cyanosis and ascites. This may occur early in the course of the disease. Usually they do not have particularly large hearts, in fact, many of them have reasonably small hearts. This patient, for a period of two years, never developed ascites. No mention is made in this record of his having had cyanosis as an outstanding clinical finding. In addition, on the basis of the law of chances, as well as on the pattern delineated here, I presume that we are dealing with rheumatic fever.

There are of course other possibilities, among them periarthritis nodosa, but that is unlikely. The lungs were said to be clear and did not show the x-ray finding that one ordinarily gets in that disease. So far as I am aware, cases of lupus erythematosus disseminatus with symptoms suggestive of Pick's disease usually have pleural thickening. I do not believe that they show so much cardiac hypertrophy as occurred here or that they have the murmurs heard in this case. In addition, this patient received all the usual treatment for heart failure. He had apparently been given salicylates for active rheumatic fever. We do not know the quantity used or the blood levels obtained. Certainly it was ineffective. All the various diuretics were ineffective. I did not mention syphilis, because the patient's age is against it, also, the serologic tests were negative. I have never seen congenital syphilis cause cardiovascular disease of any importance.

I believe this patient died of severe active rheumatic fever, with pancarditis. The electrocardiogram is rather suggestive of some pericardial disease. So I believe that, for once, Dr. Castleman has given me a straight case of rheumatic fever.

CLINICAL DIAGNOSES

Acute rheumatic fever
Rheumatic heart disease

DR. JONES'S DIAGNOSES

Acute rheumatic fever
Rheumatic heart disease, with pancarditis
Mitral and aortic regurgitation
Congestive failure

ANATOMICAL DIAGNOSES

Acute rheumatic fever
Rheumatic myocarditis, severe
Endocarditis, chronic, rheumatic, mitral and aortic
Cardiac hypertrophy and dilatation
Petechnial hemorrhages of pleura and peritoneum, with hemorrhage into peritoneal cavity

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy showed an enlarged heart, weighing 450 gm., with hypertrophy of both the right and left ventricles. The heart was somewhat flabby and dilated as well as hypertrophied. On section the myocardium was extremely soft and had a mottled yellowish-gray appearance throughout both ventricles. It was so soft that we thought that there must be definite myocardial disease, it looked like infarction except that it was not localized to one area. The mitral and aortic valves were involved, but the lesions were really slight considering the murmurs that were heard. There was only slight thickening, with no appreciable stenosis so far as we could make out, on each valve, that is, the circumference of each

valve was within normal limits. On the mitral valve there was one firm polypoid vegetation, measuring less than 1 cm. There were no nodules on the aortic valve, and there was no interadherence. I should have supposed, from its gross appearance, that the valve was competent.

Microscopic examination of the valves and the myocardium showed more Aschoff bodies than I have ever seen, every slide had a dozen or two in all stages, but most of them were acute. The valves also showed evidence of acute rheumatic fever. The pericardium was normal. The liver was enlarged and showed severe acute congestion, as did all the organs in the body. The pleura had numerous petechial hemorrhages, which one sees so often in acute rheumatic fever.

One of the interesting findings was in the abdomen. You will recall that the patient complained of abdominal pain, and that brings up the question whether there is such a thing as rheumatic peritonitis. A few papers have been written on it, but they are vague. One case has been reported in which the pathologist found active Aschoff bodies in the peritoneum*. We were unable to demonstrate any Aschoff bodies, but we did find in the lower abdomen a fair amount of fresh and old blood, as well as numerous petechial hemorrhages over the serosa of the intestines that were similar to those found in the pleura. Our sections showed acute congestion of the capillaries and veins of the peritoneum and rupture of some of them. The extravasated blood was in the gutters around the bladder; some of it was brown, indicating that it had been there for some time, perhaps a week or so. I suppose that that accounted for the abdominal pain.

DR. JONES: It is not unusual to have abdominal pain when the liver begins to go up and down like an accordion, as it did here.

DR. CASTLEMAN: You believe that the abdominal pain was due to enlargement of the liver?

DR. JONES: Most of it.

DR. CASTLEMAN: This is the first case in which we have found actual lesions in the peritoneum that might account for abdominal pain, nausea and vomiting in a patient with acute rheumatic fever.

DR. ALFRED O. LUDWIG: What about the lungs?

DR. CASTLEMAN: The lungs showed evidence of old heart failure. There were a great many so-called "heart-failure cells," but not much acute congestion.

DR. LUDWIG: Rheumatic pneumonia?

DR. CASTLEMAN: There was a little hemorrhage but not the volume that one sees in rheumatic pneumonia. The pericardium showed petechial hemorrhages but no fluid.

DR. JONES: I should like to bring out a point about the murmurs. In a heart this large, the auscultatory phenomena are not good criteria of the

*Rhea, L. J. Rheumatic peritonitis. *Am. J. Path.* 9:719-724, 1933.

amount of valvulitis. In relation to failure, the muscle damage is obviously so much more important than actual change in valvular structure that I think we overstress the murmurs in many of these cases. The present case is a good example of this point. Even in cases with real mitral stenosis, the myocardial disease itself has more effect on cardiac function than does the stenosis. We have heard all the murmurs in the acutely ill rheumatic fever patients in failure, with little valvular change at autopsy. This boy had his disease for only two years and it usually takes two, three or four years for real mitral stenosis to develop.

DR CASTLEMAN: Is it possible that the myocardial disease had some effect on the chordae tendineae, which might account for the murmurs?

DR JONES: We have seen all types of murmurs with essentially normal valves in the children who die early in the course of rheumatic fever.

DR CASTLEMAN: How does the myocardial disease produce murmurs?

DR JONES: I do not know. Pericardial disease also is accompanied by murmurs. Ring changes in the region of the base of the valves and disparity in the size of chambers probably play a role.

DR CASTLEMAN: The chordae tendineae were involved microscopically.

DR JONES: I have wondered whether there might not be an attempt at a quantitative evaluation of the Aschoff distribution. Early rheumatic failure is right-sided. It may last off and on for a long time, even two, three or four years. I do not know why this should be unless it is the disparity between the volume of the right and left ventricles and the relative greater importance of lesions in the smaller muscle of the right ventricle. This boy had left-sided failure, and hence, quantitative Aschoff body studies might be informative.

DR CASTLEMAN: Our sections showed about the same amount of severe myocardial damage on both sides.

CASE 31382

PRESENTATION OF CASE

First admission. A thirty-six-year-old man entered the hospital complaining of epigastric pain.

Two months before admission he first noted gnawing epigastric pain, radiating to the midscapular region, coming on two to three hours after meals, and partially relieved by food. Gas and distention after meals occurred, but there was no nausea or vomiting. Three weeks later he came to the Out Patient Department where, by x-ray examination, an active ulcer was demonstrated on the anterior wall of the duodenum. He was given a bland diet and belladonna, and his symptoms subsided. Two weeks later his symptoms recurred and nausea appeared. During the week before admission the pain

became much worse, interfering with sleep. There was no hematemesis or tarry stools. Physical examination was negative except for epigastric tenderness. After three weeks on an ulcer diet he was discharged improved.

Second admission (nine months later). The patient was readmitted because of recurrence of symptoms. X-ray examination showed an active duodenal ulcer, which partially healed during hospitalization.

Third admission (three years later). Two months after discharge, after an alcoholic debauch, the patient noted sharp, persistent epigastric pain, which was not relieved by alkalis. There was epigastric tenderness and spasm. The pain subsided but recurred at irregular intervals. The patient was readmitted during one of these attacks. X-ray examination revealed an active duodenal ulcer, as previously. He was discharged improved on a bland diet.

Final admission (five years later). The patient walked into the Emergency Ward at 3:00 a.m. complaining of epigastric pain of sudden onset fourteen hours previously. The pain followed the drinking of beer and was associated with weakness and prostration. The pain increased in severity but was not accompanied by nausea or vomiting or abnormal bowel movements.

Physical examination showed a well developed, well nourished, acutely ill man in severe distress. The skin was ashen. The mucous membranes were dry. The abdomen was rigid, with generalized tenderness. No peristalsis was heard. There was bilateral costovertebral tenderness.

The temperature, pulse and respirations were normal. The blood pressure was 130 systolic, 80 diastolic.

Examination of the blood revealed a white-cell count of 3800. The urine was negative. The stool was guaiac negative.

Soon after admission a laparotomy was done. Preoperative medication consisted of 11 mg of morphine sulfate and 0.4 mg of scopolamine. 24,000 units of penicillin was given intramuscularly. At operation no point of perforation was found. The anterior surface of the duodenum was covered with omentum. The abdomen was full of yellowish, viscid, odorless fluid. At the end of the operation the patient was in shock, with a blood pressure of 70 systolic, 50 diastolic. He had received intravenously 800 cc of 5 per cent dextrose in saline solution, with 5 gm of sulfadiazine. He then received the following: 500 cc of plasma, 500 cc of blood, 500 cc of plasma, 500 cc of blood, 1500 cc of 5 per cent dextrose in water and 500 cc of 10 per cent dextrose in water. He did not respond. The blood pressure did not rise above 80 systolic. He received three 11-mg doses of morphine sulfate after operation.

He became anuric and died ten hours after completion of the operation.

DIFFERENTIAL DIAGNOSIS

DR. GORDON DONALDSON I think that we all agree that this seems to be a straightforward case until the final episode. It is the story of a man of fifty-four who had had repeated x-ray proof of an anterior-wall duodenal ulcer. This ulcer had improved under medical treatment but was worse when he became indiscreet about his diet. On reading over this story of frequent recurrence of symptoms and of excessive alcohol intake, I am amazed that perforation had not occurred long before in the course of his disease. The last paragraph of the history, however, is a bit disconcerting, and I believe that, on the basis of what information we have, the presence of a perforated duodenal ulcer and peritonitis is unlikely. In the first place this patient walked into the Emergency Ward fourteen hours after what might have been perforation. Most patients are carried in when so long a time has elapsed between perforation and admission. Furthermore, I think that it is a little unusual to have a patient with a long contact with the hospital wait for fourteen hours after such a catastrophe before he appears at the hospital for help. It is a little unusual to have no nausea or vomiting. Moreover, although we have no readings of previous blood pressures, the pressure on entry was within normal limits. Of course, the white-cell count of 3800 is against peritoneal irritation from a perforated ulcer in an otherwise normal person.

At operation we have further evidence that there was no gross perforation. The omentum was adherent and may have covered a tiny perforation, but the rapidly downhill postoperative course supports the previous impression that he did not have a perforation. I shall, then, rather reluctantly dismiss the likelihood of an anterior-wall duodenal perforation on the basis of the history, physical examination, operation and postoperative course. Another fact that sways me a little bit in ruling out ulcer is that he was operated on fourteen hours after the acute episode. It is quite well established now that in operative cases of perforated ulcer the mortality rate rises rather sharply with the increase in elapsed time from perforation to suture. After twelve hours the mortality is higher than it is in patients who are ochsnerized. It has become the policy to ochsnerize patients, certainly after twelve hours and often, as a matter of fact, before the twelve-hour limit is reached, depending on their general condition. So I believe that the man who operated on this patient did not operate for a perforated ulcer.

I have listed other possibilities, perhaps in the order of likelihood. He might have had a formes frustes type of ulcer, in other words, an ulcer that had penetrated anteriorly through the bowel wall and had produced peritoneal irritation. At operation the c

of the duodenum, indicative of activity in that region. There are many points against this, however. One would expect the white-cell count to have been higher, supposing, of course, that he had a normal reticuloendothelial system. Moreover, his postoperative course was not in keeping with this sort of mild lesion. Acute gastritis can produce such severe upper abdominal pain, but I think that it can be ruled out on many of the same points as a penetrating ulcer. Pancreatitis is a likely possibility and should be seriously considered. The costo-vertebral tenderness is of interest. One of the most constant signs of pancreatitis is tenderness over the tail of the pancreas, and it is possible that the tenderness was not truly at the costo-vertebral angle, but rather over the pancreatic bed. Classically, however, one would expect a good deal of nausea and vomiting. Furthermore, the white-cell count is usually extremely high. So I am going to throw out pancreatitis and the possibility of a pancreatic stone. A pulmonary lesion, either bacterial or viral, should be mentioned but only in passing. We have no data on the chest. Appendicitis is always a possibility in a patient with upper abdominal symptoms, but I am sure that this would have been recognized at operation. He could have had a small vascular lesion in the mesentery of the small bowel. This might have been small enough to have been overlooked at operation, but I doubt it. The possibility of a malignant lesion somewhere, producing viscid fluid, should be mentioned, but I do not know where it could have been. The finding of viscid fluid bothered me considerably when I first read the history. It probably meant fluid resulting from the activity of mucus-secreting cells, and where these lay is a problem. I do not know how to explain the viscid fluid.

So I believe that we have to look elsewhere for the diagnosis, particularly in view of the dramatic postoperative downhill course. The solid parenchymatous organs ought to be considered. The one urinary examination is reported as negative. There were no liver studies. I suspect that the preoperative diagnosis was one that it was believed could be relieved by immediate operation. In retrospect, however, and reading between the lines, there are many points in favor of this patient's having liver disease of some sort. I should guess that he was more or less of an alcoholic. Or could he have had a viral type of hepatitis? The story brings to mind three cases with proved hepatitis. One patient was operated on and died, another was not operated on and died, and the third was not operated on and survived. Many features of this case remind me of these other cases. The story here, to be sure, is a little short and a little dramatic. I am not sure whether a viral hepatitis gives such a low white-cell count. The postoperative course is certainly consistent with disease in the liver. I should guess that the patient had a good deal of postoperative

discomfort and that the administration of so much morphine resulted in aggravation of the liver disease. He was given four 11-mg doses. I am suspicious of scopolamine. The use of scopolamine in a patient about whom one knows so little is debatable. It is unfair to say anything about the fluid administration. The patient remained in profound shock, in spite of the administration of 4800 cc of fluid in a rather short time. I believe that the anuria was secondary to low filtration pressure through the kidneys.

DR RODOLFO E HERRERA We certainly did not get so close to the diagnosis as Dr Donaldson has, even in the operating room. Although the patient walked into the Emergency Ward we were not impressed with his strength. He was doubled up and in acute distress. The abdomen was board-like and tender, with no peristalsis. We did not consider the low white-cell count, nor, as a matter of fact, would a negative x-ray film have made us rule out a perforated ulcer. We were sure that he had a perforated ulcer.

When we opened the abdomen in the operating room there was a great deal of fluid, which was thicker than ascitic fluid, it was turbid, had no odor and looked like gastric contents. We searched for the perforation and found that the first portion of the duodenum was hidden by adherent edematous omentum. We searched thoroughly for a perforation but thought that we should leave as much adherent tissue over the duodenum as possible since we still believed that the perforation was walled off. We had a quick look at the liver, and because we found no perforation, we paid a good deal of attention to the head of the pancreas, which appeared to be normal. The liver surface was covered with fibrin, and we believed that this change was probably due to irritation by gastric contents. We thought that it was unwise to prolong the operation, and since the blood pressure had dropped, we closed the abdomen quickly.

The patient never regained consciousness but was restless in the early postoperative course, hence the medication. The amount of intravenous fluid given was tremendous in view of the short period during which it was administered. But we had aspirated 2000 cc of fluid from the peritoneal cavity. Furthermore, if the duodenum was perforated, there would have been fluid loss into the peritoneal cavity. If this fluid contained hydrochloric acid, it would have led to peritoneal irritation and considerable peritoneal effusion. For that reason we gave over 4500 cc.

DR RONALD C SNIFFEN Did the fluid contain hydrochloric acid?

DR HERRERA We did not examine it chemically.

CLINICAL DIAGNOSIS

Perforated duodenal ulcer

DR DONALDSON'S DIAGNOSIS

Hepatitis

ANATOMICAL DIAGNOSES

Portal cirrhosis of liver, alcoholic type

Ascites

Healed duodenal ulcer

Splenomegaly

PATHOLOGICAL DISCUSSION

DR SNIFFEN At autopsy the abdomen contained 300 cc of thin turbid pinkish-gray fluid. In the region of the pylorus, duodenum and liver there were fresh fibrinous adhesions, and fibrous adhesions bound the surfaces of the liver to the diaphragm. No duodenal ulcer could be found, but in the pyloric ring there was a 1-cm area that was puckered and scarred and possibly represented a healed ulcer. The mucosa of the entire gastrointestinal tract was edematous, especially that of the duodenum and colon.

The heart was dilated, and the lungs were edematous. The spleen weighed 750 gm, about four to five times its usual size. The liver weighed 2710 gm and had the brownish-yellow hobnailed surface that is typical of cirrhosis.

Microscopic sections of the liver showed a long-standing and severe portal cirrhosis, with distorted lobules separated by a network of fibrous tissue. The process was active and seemed to have been recently aggravated, for there was an extreme fatty change in the parenchymal cells and many were degenerating. Furthermore, the mesenchymal tissue contained many lymphocytes and eosinophils but few neutrophils. In general the organ was hyperemic and edematous. A few of the liver cells contained the bright hyaline material so often seen in the alcoholic type of portal cirrhosis.

With regard to the pain, some people with cirrhosis suffer from so-called "pseudogallstone colic," which may be explained by the sudden appearance of edema and hyperemia in the organ.

DR DONALDSON How do you account for the type of fluid?

DR SNIFFEN The abdominal fluid in cirrhosis may be turbid or milky if there is a high fat content. At the time of death its character was undoubtedly changed by the irritation of operative manipulation.

DR HERRERA I should like to ask Dr Garrett if he would comment on the medication, and Dr Donaldson if he would make any exception to the rule of not operating on a perforated ulcer if it is twelve hours old or more.

DR JOHN W D GARRETT In retrospect, I believe it was unfortunate that he was given as much as 11 mg of morphine. I personally do not care to give scopolamine to a patient about whom I know nothing, although it is effective in the proper circumstances. The subsequent doses of morphine added to that already given were not ideal.

DR DONALDSON I believe that the mortality

rate following operation on patients who have perforated twelve hours previous to exploration is around 30 per cent. Several clinics have mortality figures on groups of patients who have not been operated on but rather treated conservatively by the Ochsner regime. After the twelve-hour limit the mortality figure in the latter group is lower than that in the operated group. I do not know what exception there might be to this general rule. In the operated group the mortality rises rapidly after three hours.

DR HERRERA If one is dealing with a young man, would one not be likely to accomplish something by aspirating the gastric contents from the

abdomen even later than twelve hours after perforation?

DR DONALDSON I think that generally after a certain length of time there is considerable fibrin laid down, probably the result of chemical irritation as much as anything else. This fibrin is often found sealing the right lobe of the liver over the perforation. Such a situation exists many times after six hours. After a certain length of time on conservative treatment, if abscesses do develop about the liver or in the pelvis, they can be dealt with at the proper time. If one can wait a number of days, the patient can be gotten into much better general condition for exploration, and the fluid collections will be better localized.

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PROGRESS OF BLUE SHIELD

ELSEWHERE in this issue of the *Journal* is a statement covering a recent meeting of the Subcommittee on Medical Economics of the Committee on Post-war Planning. By far the most significant action taken at this meeting pertains to the Massachusetts Medical Service, commonly known as the Blue Shield. The report that the president, Dr. James C. McCann, made to this committee deserves the careful consideration of every member of the Society. It bears testimony to the foresight of the Council in the development of the plan that was adopted and to the effectiveness with which the officers and directors of the Blue Shield have put it into effect.

It is encouraging to note that the rapid expansion of surgical and obstetric coverage may permit, in

the near future, the inclusion of medical care in hospitals without an increase in premium and that the ultimate goal is complete medical care for the low-income group.

One should not conclude that the Blue Shield as it now functions is without its critics or that it is above criticism. That these have not prevented the rapid growth of the plan is to no small degree due to the continued efforts to eliminate errors as they are found and to the co-operation of the participating physicians and their desire to make this plan succeed.

Dr. McCann's report seems to justify completely the confidence placed in him and the other officers of the Blue Shield and in those members of the Massachusetts Medical Society who have become participating physicians, and it warrants the serious consideration of those doctors who have not yet enrolled, with the hope that the list of participating physicians will soon include all members of the Society who are able to render the service offered.

FOOD RATIONING CONTINUES

THE final ending of war in Europe was unexpectedly anticlimactic to a good many Americans, others of us had evaluated it for what it was worth—the ending of the first phase of our great two-front war, a long stride toward eventual victory and the opportunity to concentrate on our most distant and our most implacable enemy.

We had realized the safety that had come so suddenly to millions of our young men—temporary for some, more lasting for others. We had seen a few returning generals riding in their well earned triumphal processions, we had made a start in bringing back our soldiers from the European and Mediterranean theaters of operations, some for their final discharge from service and others for re-deployment to the Pacific. We had had an extra trickle of gasoline for civilian use, the promise of a beginning of reconversion of industry to peacetime pursuits and a new epidemic of strikes. We had not had the rapid withdrawal and discharge from service of those who fought in Africa and Europe, we were not pouring new cars off the assembly line.

nor had we been able to relax in any degree in our food-rationing program. We were, in other words, still engaged in a major war, although considerably more weary of it than we had been, we were still rationing food and fuel and many other civilian commodities, we were still trying to control prices and avoid inflation. In short, we were attempting to combat the usual evils that accompany even a successful war.

Now, with the sudden and, to most of us, unexpected cessation of hostilities with Japan, much of our wartime economy has disappeared with a disconcerting and almost suspicious celerity. We are left with the sensation, certainly not based on facts, that restrictions that could be lifted so quickly might have been a bit overdone in the first place. Overnight, gasoline, the extreme scarcity of which (except to black marketeers) most of us had been nobly accepting, began to flow like corn and wine in Beulah Land, blue-point foods, once as tight as their namesakes, the oysters, stood naked and unashamed on the grocers' shelves, devoid of all value except a grubby commercial one, it is even hinted that red meat, for lack of which a once virile nation developed acute hepatitis, may soon be point-free.

It seems even a trifle indecent that the little hardships that we had worn, like our shabby shoes, with a certain spiritual dignity should be stripped from us. It is made to appear, almost, as if our petty luxuries represented the principles for which we had been making war and were hastily given to us, as soon as the firing ceased, before we had time to forget our bargain and to demand something more. We are still rationing foods, but not for long, and the sky's the limit on pleasure-car production again. Down with the ration book, up with the dollar sign! *Caveat emptor!* Hurrah!

MASSACHUSETTS MEDICAL SOCIETY

SUBCOMMITTEE ON MEDICAL ECONOMICS COMMITTEE ON POSTWAR PLANNING

A meeting of the Subcommittee on Medical Economics, Committee on Postwar Planning, was held on May 29, 1945. Besides the members of the subcommittee, Drs. Nathaniel W. Faxon and James C. McCann were present by invitation.

The advantages and disadvantages of the plan for the postpayment of medical fees (Blue Triangle) were discussed. It was decided to postpone a detailed discussion of this subject until a later meeting, at which time one or more men who had been active in the study and organization of this plan would be asked to meet with the committee.

The greater part of the meeting was given over to a discussion of the Blue Shield. Dr. McCann, president of the corporation, was present and submitted a report, which is reproduced below.

Following this report, there was a critical discussion of the accomplishments and future possibilities of the Blue Shield. Dr. McCann answered all questions freely and to the satisfaction of the committee. It was brought out that considerable confusion exists in the minds of both subscribers and doctors regarding the terms "limited subscriber" and "unlimited subscriber." It was brought out that the only really satisfactory way of avoiding confusion is for the surgeon to inquire of each patient for whom hospital arrangements are being made whether he is a member of the Blue Shield and, if so, whether the subscriber is a limited or unlimited one. If he is in the over-income (limited) group it should be made clear that he may expect a bill from the surgeon, toward which the Blue Shield will pay the amount allotted on the fee schedule.

The service principle of payment for medical care as used by the Blue Shield was explained by Dr. McCann, and after a detailed discussion, this was given the unanimous approval of the committee.

It was further brought out that, at the present time, the subscriber whose income is \$2000 (\$2500 with dependents) or less has all hospital, surgical and obstetric expenses paid for a period of three weeks, except the cost of x-ray examination in excess of \$15. The matter of income limits was discussed, and although no action was taken, the members of the committee thought that a \$3000 limit would probably be fairer for the man with dependents than the present one of \$2500.

In summary, the committee took the following steps: it postponed action on the plan for postpayment of medical fees, pending additional information, it unanimously indorsed the principle of prepayment of medical expenses, specifically the service principle for the under-income group as indorsed by the Council and carried out by the Blue Shield, it unanimously indorsed the plan of the Blue Shield to extend coverage to include medical care of patients in hospitals as soon as it has met the requirements of the Commissioner of Insurance, and it recommended that all licensed physicians who are able to render the service offered should support and participate in this plan for the development of medical service to the community.

LELAND S. MCKITTRICK, *Chairman*

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REPORT ON MASSACHUSETTS MEDICAL SERVICE

Growth

The growth of Massachusetts Medical Service, established by the Massachusetts Medical Society, has assumed proportions that appear to assure it future success. By July, 1945, there will probably be enrolled 150,000 subscribers in about 1600 groups. A recent survey shows that Massachusetts had a larger net enrollment for the first quarter of this year than any other medical-society plan in the country.

The financial condition of the corporation is equally satisfying. The established premium rates have made possible full delivery of all designated services, the payment of service fees in full to physicians and the steady accumulation of a substantial reserve. Shortly after establishing the program, it was apparent that all restrictions on pre-existing surgical conditions could be removed, and this has eliminated endless irritations for both the subscriber and the physician. Even after this step, the corporation successfully placed aside every month the 25 per cent of premiums required by the Commissioner of Insurance as a reserve. After setting aside this reserve, after paying in full for all professional services and after meeting all administrative expenses, there is still a surplus of about 5 per cent of the total income, which comprises a second reserve fund.

There are two basic reasons for this satisfactory result. First and foremost are the co-operation and confidence manifested by the majority of the profession in the Blue Shield. This happy state, unfortunately, has not characterized the ventures in some of the other states. Nearly four fifths of the actively practicing physicians in Massachusetts have signed contracts of participation in the program. Even the medical men, who have not as yet received benefits from the corporation, have willingly joined. This evidence of full support by the profession has been of paramount importance in promoting public support in our endeavor, and the enrollment figures are beginning to reflect public confidence.

The second basic reason for the satisfactory result is the healthy and rational relation that we have maintained with the Blue Cross. On both sides there have been questions and some controversy, but these have always been satisfactorily resolved, and the basis of mutual good faith in our dealings has been sedulously protected on both sides. With their guidance, unnecessary and fancy extensions of overhead expense have been avoided, which accounts in a large measure for our healthy financial state. Mr. Cahalane, executive secretary of the Blue Cross, is also executive secretary of the Blue Shield. Within recent months Mr. Cunningham, of the Blue Cross, has been assigned to devote all his time to the interest of the Blue Shield. The clearing of medical accounts is handled in an expeditious manner by Mr. Gilbreath, of the Blue Cross, and two secretaries. All matters not in the fee schedule are referred to special committees of physicians, and their findings are used. It is significant that 150,000 subscribers and 4500 physicians can have their medical-care services administered by the already established facilities of the Blue Cross with a few additional persons. This fact may well serve as an object lesson to other states undertaking a program to avoid heedlessly plunging into overhead expense from unnecessary duplication of administrative organization.

Extension

The established surplus indicates that by July, 1945, we shall have accumulated the \$225,000 surplus required by the Commissioner of Insurance before expansion. It appears from actuarial study that medical care in the hospital may be added to the contract without increasing the premium rate. This whole problem will have to be studied by a committee of internists and general practitioners, and approval by the Commissioner of Insurance will have to be procured. It is gratifying to be in a position to make a move that will justify the confidence that the medical men have shown in the program from the beginning. Our ultimate obligation to extend the program to include at least some portion of medical care in the home and office is still kept in mind.

Income Limits

The question of the method of determining the income of subscribers as related to the income limitation for service contract was explored. It was pointed out that industry, which provides payroll deduction for the workers, will go

only so far in exposing incomes of workers. At present, when the program is presented to a group of prospective subscribers, the matter of income limits for the service contract is explained. On the back of the card they must indicate whether their total family incomes are above or below the limits. In this we have to proceed on the assumed truthfulness of their statements. In instances in which false statements have been made, industry so far has been willing to verify income for the protection of the physician and the corporation. Discussion established to the satisfaction of the committee that costs and administrative problems would make it impossible for the Blue Cross to check constantly on income changes of the individual subscribers. The report a physician receives, however, states whether, at the time of enrollment, the subscriber was a limited (over-income) or an unlimited (under-income) person. The physician is free to investigate any change of status from the time of enrollment. It was agreed that the proper place for determining any change is in the doctor's office. In response to further questions it was brought out that, for the present, a graduation of premiums to meet a graduation of incomes is not practicable.

Service Contract

The committee was informed that Massachusetts is one of the few states which, without reservation, has put into effect a bona fide service contract for the lower-income group. There are no extra payments to the physician by the corporation, there are absolutely no payments by the corporation to any nonparticipating physician, by and large there is no apparent overcharge to the low-income group by the participating physician. In the few instances in which this has occurred, the industries have advised their workers that they do not have to pay. There seems to be a tongue-in-the-cheek attitude on the part of some men in the headquarters of the American Medical Association about the service type of contract. This attitude, unfortunately, has infected some of the state plans, so that they have undertaken a meaningless cash-indemnity insurance business. In the long run this will not satisfy the public, industry, labor or health groups who rightly seek bona fide protection for the under-income group by a prepayment service contract. Cash indemnity is a sham that imposes no obligation of restraint on the profession in its financial relations with the under-income group.

JAMES C. McCANN, President
Massachusetts Medical Service

NEW HAMPSHIRE
MEDICAL SOCIETY

DEATHS

JOYCE — Roland J. Joyce, M.D., of Nashua, died July 8. He was in his fiftieth year.

Dr. Joyce received his degree from Tufts College Medical School in 1920. He was a member of the Nashua and the Hillsborough County medical societies and served as president of the latter.

His widow, two daughters and two sons survive.

TARBELL — Wallace H. Tarbell, M.D., of Contoocook, died July 20. He was in his seventy-fourth year.

Dr. Tarbell received his degree from the University of Vermont College of Medicine in 1902. He was a fellow of the American Medical Association.

His widow survives.

NOTICES

NEW ENGLAND ROENTGEN RAY SOCIETY

A meeting of the New England Roentgen Ray Society will be held at the Harvard Club of Boston on Friday, September 21. There will be an x-ray conference at 4:30 on the topic "Diseases of the Gastrointestinal Tract," conducted by Drs. Chester M. Jones and Robert G. Vance. At 8:00 p.m., the following program will be presented:

Pneumonoconiosis Dr. Louis Benson

Pulmonary Embolism Dr. Felix G. Fleischer

Interested physicians are invited to attend.

(Notices continued on page xvii)

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HODGKIN'S DISEASE*

V. Involvement of Certain Other Organs

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BOSTON

THE preceding article covered the involvement of the hilar nodes, lungs, gastrointestinal tract, bones and skin by Hodgkin's disease. In this paper the involvement of certain other organs will be discussed.

LYMPH NODES

Hodgkin's Paragranuloma

In Hodgkin's paragranuloma, the peripheral lymph nodes, most frequently those in the neck, are invariably involved. Indeed, the initial symptom of the condition is almost always peripheral lymphadenopathy. The mediastinal lymph nodes are involved in approximately one third of the cases. Unless such mediastinal involvement is massive or there are indications that the condition is progressing into Hodgkin's granuloma, the prognosis is not necessarily poor.

Hodgkin's Granuloma

In Hodgkin's granuloma, lymphadenopathy in one region or another often brings the physician's or the patient's attention to the presence of the disease. By far the most frequent site for lymphadenopathy

The superficial lymph nodes in one or another part of the body sooner or later are almost invariably involved, and it has already been noted that by far the most frequent initial symptom is cervical lymphadenopathy, although this may not be noticed by the patient. The characteristics of the enlarged nodes have already been referred to.

There is some disagreement among investigators concerning the most frequent sites of the lymphadenopathy, the source of confusion often being failure to state whether clinical or autopsy material is referred to or whether the author is recording merely the lymphadenopathy encountered when the patient was first seen or that which may have occurred later in the course of the illness.

Of our 213 cases, 174 have been carefully followed to date or to death. The distribution of enlarged

TABLE 2 *Lymphadenopathy During the Course of Hodgkin's Granuloma in 174 Cases*

LYMPHADENOPATHY	No. of Cases
Cervical	149
Axillary	112
Mediastinal	90
Inguinal	73
Abdominal	33
Epitrochlear	10

lymph nodes as observed clinically is seen in Table 2.

In 14 patients there were no palpable lymph nodes except in the cervical area at any time during life. Of these, 1 is alive and apparently well twenty-four years after the onset of his disease. The course of the other 13 cases did not differ materially from the general average. In 2 cases, the enlarged nodes were limited to one inguinal region. One of these patients died after four years, the other is alive, following a groin dissection, five years after onset. In 2 cases only were the lymph nodes apparently limited to the mediastinum. It is of some interest that each of these patients died within a month of his first symptom, dyspnea.

In some cases, a varying degree of cervical lymphadenopathy was present over a long period of

TABLE 1 *Initial Lymphadenopathy in 213 Cases of Hodgkin's Granuloma*

LYMPHADENOPATHY	No. of Cases
Cervical	154
Axillary	27
Inguinal	15
Mediastinal	4
None	13

at the onset is in the neck, and as has already been pointed out, mediastinal enlargement without peripheral lymphadenopathy is extremely rare (Table 1).

*From the Thorndike Memorial Laboratory, the Second and Fourth Medical Services (Harvard) and the Mallory Institute of Pathology, Boston City Hospital; the Department of Medicine, Harvard University, and the Pondville Hospital, Massachusetts Department of Public Health. This is the fifth of a series of seven papers covering the various aspects of Hodgkin's disease.

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time without causing any symptoms. A sudden increase in the size of the nodes then caused the patient to seek medical advice. It is impossible to say in these cases whether the condition was true Hodgkin's granuloma from the onset, whether the initial lymph nodes were merely inflammatory or whether they represented one of the precursor pathologic conditions, such as Hodgkin's paraganuloma, or giant-follicle lymphoma. In any event, the persistence of cervical lymph nodes in adults, even if they vary greatly in size from time to time, demands much more serious attention than is often accorded it. This matter has already been referred to under "initial symptomatology" in one of the previous papers of this series. One further case may be cited here.

E H P (H 29-831), a 46-year-old man, was admitted to the hospital on June 25, 1929. His mother had died of tuberculosis and his father of "carcinoma." The past history was unimportant.

In 1919, the patient noticed a small, nontender lump in the right axilla. This varied greatly in size, at times being as large as a walnut and at others no larger than a bean. Five years later this mass was excised by his family physician, but no further treatment was advocated and no pathological study was made. The patient continued to feel well until 1928, when he noted increasing constipation and some pain, unrelated to defecation, in the region of the coccyx. Early in January, 1929, the pain became worse and "spread throughout the rectum." The constipation continued, and in the next 6 months he lost 18 pounds, although his appetite remained good.

Physical examination on admission showed marked tenderness over the symphysis pubis and the lower part of the sacrum. There were several large, firm, freely movable lymph nodes in the right axilla. X-ray films of the gastrointestinal tract and lungs showed no abnormalities, but did reveal a destructive process in the sacrum "probably due to Hodgkin's disease." Rectal examination was negative. A node was removed from the right axilla and showed the typical lesion of Hodgkin's granuloma.

In the course of the next 2 months, 1200r was given over the sacrum and pelvic region, but the patient continued to lose weight rapidly and died on August 11. No autopsy was obtained.

The nature of the cervical lymphadenopathy that continued, with remissions and relapses, from 1919 to 1929 in this case is, of course, uncertain, but it is our belief that, in adults, notably enlarged lymph nodes, unless associated with obvious infection, are almost always tuberculous or cancerous, and one cannot help speculating what the course of the disease would have been had a radical dissection of the axilla, followed by intensive x-ray therapy, been carried out in 1919.

In other cases, proved tuberculous adenitis has preceded by months or years the development of Hodgkin's granuloma in the same region. This sequence of events was seen in 6 of these 213 cases.

Desjardins and Ford¹ have stressed the relation of infected teeth and tonsils to the appearance of Hodgkin's granuloma in the cervical region, but the great frequency of such pyogenic infections, the comparative rarity of Hodgkin's granuloma of the tonsil, the frequency of involvement of the posterior

triangle in that disease and the relative frequency of the involvement of the axillary and inguinal lymph nodes seem to argue against any direct etiologic relation. It is perhaps likelier that acute upper respiratory or oral infections simply light up an already existing dormant disease or bring to the attention of the patient lymph nodes already enlarged but otherwise symptomless.

Axillary and inguinal lymph nodes due to Hodgkin's granuloma are more likely to be painful from their position than those in the neck, but otherwise they do not differ in their characteristics. Epitrochlear nodes, although traditionally associated with secondary syphilis and often secondary to obscure infections of the hand, are sufficiently often due to Hodgkin's granuloma to demand serious attention. Indeed, it may safely be said that any lymph node materially enlarged over a period of time and unassociated with infection in an adult should receive a biopsy. On the other hand, it is extremely unusual for Hodgkin's granuloma to occur without the presence of superficial lymph nodes at some time or another during its course. We entirely agree with the following statement by Baker and Mann:²

Hodgkin's disease of deep structures unassociated with superficial glandular enlargement is rare. In view of the frequency with which a diagnosis of Hodgkin's disease is made in cases of mediastinal tumor, of splenomegaly and so forth, a diagnosis often proved wrong by subsequent events, we deprecate the diagnosis of Hodgkin's disease in the absence of histological evidence obtained by biopsy of superficial lymph glands. If no superficial glands are obtainable during the course of the disease, the case is probably not one of Hodgkin's disease.

The obvious exceptions to this general rule serve only to accentuate its importance.

Hodgkin's Sarcoma

In Hodgkin's sarcoma, the presence of enlarged superficial lymph nodes when the patient first comes to the physician's attention is by no means so frequent as it is in Hodgkin's granuloma. Indeed, in

TABLE 3 Initial Lymphadenopathy in 32 Cases of Hodgkin's Sarcoma

LYMPHADENOPATHY	No. OF CASES
Cervical	10
Axillary	5
Inguinal	3
None	14

nearly half of our cases such peripheral initial lymphadenopathy was absent (Table 3).

Peripheral lymphadenopathy is usually although not invariably present during the course of Hodgkin's sarcoma (Table 4). The very generalized peripheral lymphadenopathy so frequent in Hodgkin's granuloma is seldom seen. Mediastinal lymph nodes

are involved in approximately one third of the cases, although massive involvement is rare. It should be recalled that the disease frequently starts in the

TABLE 4 *Lymphadenopathy During the Course of Hodgkin's Sarcoma in 32 Cases*

LYMPHADENOPATHY	NO OF CASES
Cervical	21
Axillary	19
Inguinal	15
Mediastinal	10
Abdominal	9
Epitrochlear	6

retroperitoneal lymph nodes, and these, of course, are not readily felt during life

TONSILS AND NASOPHARYNX

Hodgkin's Paragranuloma

Involvement of the tonsils and nasopharynx does not exist in Hodgkin's paragranuloma

Hodgkin's Granuloma

Hodgkin's granuloma rarely involves either the tonsils or the nasopharynx. In but 6 of our 213 cases was there such involvement. In 1 there was a large, translucent mass in the posterior pharynx. In the remaining 5, a tonsil was involved unilaterally by a mass described as whitish or translucent. The surface was occasionally ulcerated. In each case, the involvement of the tonsil occurred early in the disease and was almost invariably accompanied by notable cervical lymphadenopathy. This fact reflects the rapidity with which this form of the disease advances. New and Childrey,² in a comprehensive study of certain tumors of the tonsils and pharynx, found that 59 per cent of the patients had enlarged cervical lymph nodes when first seen.

The serious nature of this condition and the ease with which, by contrast, it may be confused with more innocent affections of the throat require more than passing notice.

The age of the patients in this series varied greatly, the youngest one being seven and the oldest seventy-nine. The median was forty-four years. The symptoms were varied, including cough, dysphagia, persistent sore throat and hemoptysis. Five patients died of generalized Hodgkin's granuloma in less than two years from the time that the involvement of the tonsil or pharynx was noted. The remaining patient was, in a sense, more fortunate.

W. W. (P 8212), a 79-year-old man, noticed in May, 1934, a soreness in the left side of the throat, together with an enlargement of the left tonsil. Gargles and hot applications did not seem beneficial, and he was admitted to the hospital on June 26, 1934. Physical examination at that time revealed a well developed and well nourished elderly man. There was a firm, opalescent tumor, measuring 5 by 3 by 3 cm, arising from the left tonsil. There was no cervical lymphadenopathy, and the remainder of the physical examination was essentially normal for a man of his age.

The red-cell count was 4,060,000, the hemoglobin 80 per cent, and the white-cell count 10,600, with a normal differential count. X-ray examination failed to reveal any disease in the heart, lungs or bones.

The tumor was removed as completely as possible, and radium seeds were implanted in the underlying fossa, a total of 528 mc hr being given. In addition, during the next 2 months a total of 1200 r (250-Kv machine) was given to the left cervical region. There was no recurrence of the disease, and the patient died of heart failure in January, 1940, more than 5 years after onset.

It is admittedly rare to see such a localized lesion, yet the cases illustrate the necessity of careful inquiry into the causes of sore throat in elderly persons and the advisability of employing to the fullest extent all therapeutic measures, even in the face of an apparently hopeless situation.

Hodgkin's Sarcoma

Involvement of the tonsils and nasopharynx by Hodgkin's sarcoma is not rare, it occurred in 11 per cent of our cases. In 3 of these the tonsil was involved, and in 1 the palate and antrum. The most frequent initial symptoms are localized pain, nasal obstruction, tumor in the throat and sore throat. In addition, during the course of the disease, loss of weight is almost invariable, and dyspnea, sometimes due to nasal obstruction, is not infrequent.

The tumor is highly invasive and destructive, and patients afflicted with this type of involvement live but a short time. None of those in this series lived over three years after onset. The tumors of the tonsil have, in our experience, been extremely large and ulcerated, and although they usually have responded well to initial irradiation recurrence has been rapid and later irradiation has had but little effect. In 1 case, there was a bluish tumor over the hard palate that rapidly extended, destroying the surrounding bone and filling the right antrum. In spite of irradiation, there was subsequent extension into the right nostril, with death ensuing shortly.

The following case may be cited as an example of this type of infiltration.

P. G. (HH 24-806), a 45-year-old man, was admitted on June 27, 1924, with a chief complaint of sore throat. In the previous April he had noticed a growth in the throat and felt generally weak.

Physical examination on entry showed a large, sloughing tumor involving the right tonsil and extending up into the nasopharynx. In addition, there were several enlarged, non-tender lymph nodes in the right side of the neck. Eight seeds of 1 mc each were inserted into the tumor tissue. Within a week the growth had disappeared to a great extent, but 9 months later the left tonsil became enlarged to such an extent that it filled almost the entire pharynx. Four 1.5-mc. seeds were inserted into the tumor, with good local results, but there was a residual enlargement of the lymph nodes in the left side of the neck. A moderate amount of x-ray therapy was directed toward these, with but little effect.

The patient was constantly tired. The nares were almost completely obstructed by the tumor, and there was a troublesome productive cough and a severe sore throat. In addition, there was a distressing generalized headache. He developed marked exophthalmos and ptosis of the left eye and, in spite of x-ray therapy, died 5 years after the first symptom.

Autopsy Post-mortem examination showed Hodgkin's sarcoma involving the right tonsil, with direct extension to the nasopharynx and the sphenoidal sinus and involvement of the pituitary gland, the right orbit, the right temporal bone and the adjacent dura

LIVER AND SPLEEN

Hodgkin's Paragranuloma

In 21 per cent of our cases of Hodgkin's paragranuloma, enlargement of the spleen was noted during life, and progressive enlargement of this organ has been, in our experience, an ominous sign. Enlargement of the liver practically never occurs.

Hodgkin's Granuloma

Both the liver and spleen are frequently enlarged in Hodgkin's granuloma. From a study of the reported cases, Wallhauser⁴ came to the conclusion that hepatomegaly was present in about 50 per cent of the cases and splenomegaly in approximately 70 per cent. Uddströmer⁵ found slightly lower figures — 36 per cent for the liver and 63 per cent for the spleen.

In our own cases followed to date or to death, the liver was enlarged in 30 per cent and the spleen in 56 per cent. It is probable that these figures are too low.

Only rarely does either organ reach massive size. In spite of the frequency with which these organs are involved, symptoms referable to them are surprisingly rare. Ascites was present in but 11 of our 62 cases with hepatomegaly, and jaundice occurred in only 6. Splenomegaly occasionally reaches massive proportions without causing any symptoms whatever, but it is not infrequent for patients in whom the spleen is greatly enlarged to complain of a dragging sensation in the left side of the abdomen, and occasionally an enlarged spleen causes acute pain, particularly if there is an associated perisplenitis.

It is well recognized that the size of the spleen may increase greatly in the presence of fever, and indeed it may be palpable only during periods of pyrexia. It is not so well known that an enlarged spleen may diminish in size without any treatment whatever. All in all, enlargement of these organs, although frequent, does not appear to have great clinical importance, except in so far as it indicates the generalized nature of this condition.

Hodgkin's Sarcoma

In Hodgkin's sarcoma, enlargement of the liver and spleen occurred — always coincidentally — in 38 per cent of our cases. Rarely, however, is there great enlargement of either organ at autopsy, and their involvement does not appear to contribute materially to one's knowledge of the future course in any given case. In 2 cases the liver extended to the level of the umbilicus or lower, and in 1 the spleen reached nearly to the iliac crest.

SEROUS CAVITIES

Hodgkin's Paragranuloma

Involvement of the serous cavities does not occur in Hodgkin's paragranuloma.

Hodgkin's Granuloma

In Hodgkin's granuloma, pleurisy with effusion is frequent. Evidence of fluid within the pleural cavity was found in 35 of such of our cases as had been followed to date or to death. In 8 of these, the fluid was present bilaterally. In the great majority of cases it appears to be dependent on involvement of the mediastinal nodes, much more rarely it is secondary to granulomatous lesions of the pleura. Versé⁶ was of the same opinion. Occasionally it is tuberculous in origin.

In 6 of our cases, the effusion was bloody, in 1, it was chylous and apparently due to tuberculous invasion of the thoracic duct, and in 1 a colon-bacillus empyema had developed as a result of a fistulous tract that perforated the diaphragm and connected the colon with the pleural cavity through a series of necrotic nodes. All other effusions were serous.

The amount may be small, and the fluid may disappear after one or two taps and appropriate x-ray therapy to the mediastinum. Oftener, unfortunately, the amount of fluid is large and repeated thoracenteses are required for adequate relief. Under these circumstances, the eventual subsidence of the effusion depends very largely on the response of the hilar and mediastinal nodes to radiation therapy. In this connection, one point is perhaps worthy of passing comment. The diaphragm is frequently elevated in the presence of a mediastinal tumor, and it may remain high after the subsidence of the mass so that by cursory examination there are still signs highly suggestive of fluid. In 1 of our cases, death resulted from a lack of recognition of these facts. Four years previously, the patient had had a mediastinal tumor and a massive effusion on the left. Under x-ray therapy these had subsided, but the left diaphragm had remained greatly elevated. Under the impression that fluid still existed, a needle had been introduced into the chest by a physician unfamiliar with the patient's history, the diaphragm was perforated, and death resulted from hemorrhage from a lacerated spleen.

In our experience, pleural effusions may develop at any time during the course of the disease although they are usually late. They do not appear to have any definite bearing on the prognosis.

Baker and Mann² describe spontaneous pneumothorax. This complication we have not seen.

It is generally agreed that the peritoneum is but rarely implicated directly, and likewise ascites is a rather infrequent complication.⁵ We have found clinical evidence of ascites in only 5 per cent of our

cases, and in all but 1 of these the complication was terminal and was followed by death within a month or six weeks. In this single case, ascites was present intermittently for a year prior to exitus, but it appeared to be dependent on cardiac failure rather than on granulomatous involvement of the peritoneum. In another case, a massive ascites developed terminally and was shown at autopsy to have been due to alcoholic cirrhosis of the liver. It is always well to remember that a patient with Hodgkin's granuloma may in addition have some other major disease. Our own failure to recognize this fact has, in one or two cases, been unfortunate. Ascites should be regarded as of serious import unless occasioned by remediable factors.

We have encountered pericardial effusion during life in only 2 cases. In each, the fluid was hemorrhagic and death ensued shortly after its clinical recognition.

Hodgkin's Sarcoma

Pleurisy with effusion is also not infrequent in Hodgkin's sarcoma. In our own series, it occurred in 7 (22 per cent) of the cases during life. In 6 of these, the fluid was grossly bloody. This is in sharp contrast to the character of the pleural fluid of Hodgkin's granuloma, which, as we have said, is usually serous. In Hodgkin's sarcoma, the effusion is usually associated with involvement of the lungs. In several cases, however, there was no evidence during life of involvement of either the lungs or the mediastinal lymph nodes. It is not improbable that in these cases there was direct implication of the pleura itself by the neoplastic process. The effusions, whether sanguineous, serous or purulent, have invariably been extremely large in amount and not seldom have required frequent thoracenteses.

Ascites occurred in only 2 cases.

We have never seen pericarditis with effusion.

NERVOUS SYSTEM

Hodgkin's Paragranuloma

Involvement of the nervous system is never seen in Hodgkin's paragranuloma.

Hodgkin's Granuloma

In Hodgkin's granuloma, signs and symptoms referable to the cord or peripheral nerves are not unusual. Actual invasion of the brain substance or cord is extremely rare.^{7,8}

Cortical manifestations are infrequent. Johnsson⁸ found only 8 cases exhibiting cerebral symptoms among 37 that had some involvement of the nervous system. Epileptiform seizures are, however, occasionally seen, and appear in practically all cases to be due to invasion of the dura. So far as we are aware, there is only 1 case reported in the literature in which a granulomatous lesion was found in the

substance of the cortex. Von Hecker and Fischer⁹ describe in some detail the case of a thirty-two-year-old man suffering from what appeared clinically to be widespread Hodgkin's disease. A few days before death he had several epileptiform seizures, followed by deep coma. At autopsy there was found in the region of the centrum semiovale a cherry-sized granulomatous focus that showed a histologic picture extremely suggestive of Hodgkin's granuloma. Even in this case, however, some question may be raised whether the cortical lesion was actually Hodgkin's granuloma, for earlier biopsy of an axillary lymph node had shown small round-cell sarcoma, and according to the authors themselves many of the involved organs failed to show a clear-cut histologic picture. Johnsson has been erroneously quoted in the literature as describing cortical lesions, but he specifically points out that in no case other than that of von Hecker and Fischer⁹ was there any histologic evidence of involvement of the brain substance. Among our patients, there was 1 who exhibited terminally signs of increased intracranial pressure, choked disks, rotatory nystagmus, progressive coma and death. Unfortunately, no autopsy was obtained. Terminal headache, convulsions and coma are frequent, their cause is obscure.

Symptoms referable to the spinal cord are relatively frequent.^{3,8,10,11} One patient died in coma following the rapid development of a meningitis.

W. A. (BCH 346957), a 35-year-old man, was admitted on November 22, 1916. In 1911 he noticed enlargement of the lymph nodes in the left side of the neck and the left axilla. For the next 5 years, the swellings gradually increased in size, particularly during the winter months. In the month of admission, he noticed gradual swelling of the abdomen. His general condition remained good.

Physical examination on admission showed many firm lymph nodes in the left side of the neck and the left axilla. There were signs of fluid in the right pleural cavity, and ascites was also present. The veins over the lower abdomen were enlarged. The temperature, pulse and respirations were normal. The red-cell count was 5,400,000, the hemoglobin 75 per cent, and the white-cell count 3500, with 50 per cent neutrophils, 15 per cent lymphocytes and 35 per cent monocytes. The platelets were normal. The patient was comfortable and up and about the ward.

Six weeks after admission, the patient suddenly screamed and fell to the floor. Thereafter there was deepening coma, and the temperature rose to 105°F. There were no pupillary changes and no paralysis. Death occurred on January 5, 1917.

Autopsy. Post-mortem examination showed Hodgkin's granuloma of the cervical and axillary lymph nodes and of the spleen, central necrosis and regeneration of the liver, ascites, bloody fluid in the pericardial sac and acute meningitis. In the foramen magnum and beneath the right temporal lobe there was 75 cc. of brownish mucopurulent fluid. The pial vessels were slightly injected. The brain, pons, medulla and pituitary were normal, except that on the pia over the cortex, basal ganglia and dorsal cord microscopic examination showed a moderate amount of seropurulent exudate. Cultures of the brain and cord yielded a beta-hemolytic streptococcus. No origin of the meningitis was found.

Although actual granulomatous lesions arising within the substance of the cord are extremely rare,

if indeed they exist, neurologic symptoms may be produced in various ways

In the first place, epidural or subdural granulosomatous deposits may surround and press on the cord

Secondly, there may be pressure from lesions arising in the vertebrae or from collapse of vertebral bodies that have been destroyed by the disease. In 92 per cent of Weil's¹⁰ cases, the symptoms could be traced to dural lesions or those in the spine itself. Sudden death has been reported from dislocation of the diseased spine and severance of the cervical cord.¹² In our series, the evidence points to bone lesions as being the most frequent source of cord symptoms

Thirdly, there may be compression or actual invasion of the vessels and lymphatics of the cord by tumor from the adjacent lymph nodes. Weil¹⁰ in particular has stressed this type of involvement. He writes

The mechanism of the myelopathy can easily be explained by the mechanical obstruction of blood vessels and lymphatics supplying the spinal cord through the lympho-granulomatous tissue, either within the intervertebral foramina or outside the spinal canal. It can easily be understood that the interruption or diminution of vascular supply of the spinal cord, if continued over a longer [sic] period of time, will produce a diffuse myelomalacia, which will be the more severe the more spinal arteries are involved

Fourthly, there may be a meningitis.³

And, finally, there may be a toxic myelitis of uncertain nature. Allen and Mercer¹¹ in particular have stressed this origin of the spinal symptoms. Gordon¹³ and others demonstrated that the intracerebral inoculation of rabbits with emulsions of tissue derived from cases of Hodgkin's granuloma produced signs of ataxia, muscular spasms and paralysis. Examination of the cord in such animals reveals few definite lesions. The fact that in experimental animals and in some clinical cases there is a marked disparity between the severity of the clinical manifestations and the paucity of the findings on anatomic or histologic examination raises the interesting speculation whether, in man, certain cases of paralysis may not be due to some ill defined toxin derived from the granulomatous tissue. The possibility cannot be denied, yet extremely careful study at autopsy would be necessary to rule out invasion of the dura or epidural space and lymph nodes pressing on afferent blood vessels. It has recently been demonstrated that the Gordon phenomenon is due to the presence of eosinophils,¹⁴ and in this connection it is worthy of note that in both the cases described by Allen and Mercer¹¹ there was an eosinophilia, amounting in 1 case to 78 per cent.

Nine of our 174 cases, on which we have complete clinical data, showed evidence of paralysis of the legs. In 7, the paralysis was flaccid, in 2, it was spastic. In all 9 cases there was diminution or absence of tactile sensation, and in all there was some disturbance of the rectal and vesical sphincters. In

all, the point of origin appeared to be in the dorsal segments. In Weil's¹⁰ series, the dorsal region was involved in 80 per cent, the cervical in 16 per cent, and the lumbosacral in 4 per cent. Weil regarded paralysis as a late and almost invariably fatal complication. In over 80 per cent of his collected cases the patients died within three months after the appearance of the neurologic symptoms, and none survived more than a year after the onset of the paralysis. That the prognosis is not always so grave is attested by the fact that 3 of our 9 patients survived more than a year after the paresis or paralysis had set in, and 1 was alive and in comparatively good health four years later.

J. C. (HJ 1-30), a 35-year-old policeman, in the early part of 1930 noted enlarged painless lymph nodes in the left side of the neck. A biopsy at that time showed the typical picture of Hodgkin's granuloma. X-ray therapy was instituted, and the nodes promptly subsided. In 1933, the patient developed a mediastinal tumor and a left-sided pleurisy with effusion. Under x-ray treatment and after several chest taps, the mediastinal mass subsided and the fluid disappeared. He remained in fairly good health.

Early in July, 1935, the patient suddenly developed weakness and numbness of both legs. A few days later, he became completely paralyzed from the waist down. There was no pain. He had some difficulty in starting the urinary stream, but no incontinence. The abdominal and cremasteric reflexes were absent. The knee jerks and ankle jerks were equal and hyperactive. There was a bilateral Babinski sign and sustained clonus. No movement could be made from the waist down. Tactile sensation was markedly diminished, and pain sensation was absent below a line parallel with the nipples anteriorly and the midscapula region posteriorly. Lumbar puncture showed evidence of complete block. The initial pressure was equivalent to 160 mm of water. There was no rise on jugular pressure. Coughing or straining caused a rise to 310 mm. The spinal fluid was clear and colorless, with 2 lymphocytes per cubic millimeter. The Pandy test was strongly positive. No gold-sol curve was done.

X-ray studies of the spine revealed no definite abnormalities. There were numerous small, shotty lymph nodes in each side of the neck, each axilla and each groin. The heart appeared to be normal. The left diaphragm was markedly elevated. The abdomen was normal. There was no fever.

High-voltage x-ray therapy was immediately begun over the dorsal spine. Within 3 weeks there was less difficulty in passing urine and tactile sensation began to return. By August 8, approximately 1 month after the onset of the paralysis, the patient was able to move his legs slightly. By the end of August, the improvement was marked, and he was able to move his legs in all directions, though he was unable to bear any weight on them. There were still bilateral Babinski signs and ankle clonus. From that time on, improvement was slow but continued. By June, 1936, a year after the paralysis set in, he was able to walk with crutches, and by October of the same year he could walk without assistance. His general condition was good. Sensation had become normal, and the only abnormal neurologic finding was that both knee jerks and ankle jerks were hyperactive. From July, 1935, to October, 1937, he had received a total of 4300 r (250-kv. machine) to the dorsal spine. In September, 1937, he developed a broad band of herpes zoster corresponding to the distribution of the fourth thoracic spinal nerve on the right. After 3 weeks this cleared, leaving a broad scar, as herpes usually does when due to Hodgkin's granuloma.

The patient was able to return to duty as a sergeant in the police force, and although his legs were somewhat weak, he remained active until his death by accident in May, 1939, nearly 3 years after the onset of the paralysis.

No autopsy was performed in this case, and the cause of the symptoms must therefore remain a matter of conjecture. It is probable, however, that

granulomatous tissue had extended from the para-aortic nodes through the intervertebral foramina to surround and compress the cord, and this supposition is somewhat strengthened by the development of the herpetic lesion in the upper dorsal region, for it has been suggested by many that herpes in Hodgkin's granuloma is due to pressure on the spinal roots by granulomatous tissue

In this case, no gold-sol curve was done on the spinal fluid, nor have we seen any such determinations reported in the literature. In other cases in this series, however, in which there was paralysis associated with Hodgkin's disease or some other form of lymphoma the spinal fluid has shown a midzone curve suggestive of syphilis or early multiple sclerosis. Under x-ray therapy, the curve has usually flattened out or shown a tendency to less marked midzone rises

In 5 of the other cases in this series in which there was paralysis of the legs, there was marked destruction of the thoracic and lumbar vertebrae, and it seems reasonable to assume that the paralysis was due either to pressure on the cord from collapsed vertebrae or to pressure from surrounding granulomatous lesions that had coincidentally invaded the vertebrae. There was, however, no autopsy confirmation of this supposition. In 2 cases, paralysis was secondary to meningitis. In one of these, a *pyocyaneus-bacillus* meningitis apparently originated from a fistulous tract extending through necrotic lymph nodes from the intestine to the spinal canal. In the second, there was a torula meningitis of uncertain origin

Symptoms referable to peripheral nerves are frequent. Abdominal pain often seems to originate in this fashion, perhaps owing to pressure on dorsal roots. Less often there is pain in the face, neck, arms or legs. Herpes zoster is a not infrequent complication and usually leaves a scar after its subsidence. Exophthalmos and enophthalmos are occasionally encountered. Rarely the cranial nerves are implicated.¹⁵

Hodgkin's Sarcoma

Involvement of the central nervous system in Hodgkin's sarcoma is not frequent. We have seen 3 cases involving the cerebellum, but unfortunately the post-mortem examination in each case was limited to the head

In view of the rarity of this condition it may not be amiss to include one of the case histories

P. L. (BCH 1049224), a 65-year-old Italian, was admitted on September 10, 1941, in an unconscious state. He had been well until March, 1941, when following a minor injury he became shaky and staggered while walking. These symptoms forced him to quit work about the end of July. They increased gradually during the ensuing months, and in early September his speech became thick and mumbly. In addition, he complained of difficulty in swallowing. At approximately the same time, the right eyelid tended to droop. He became stuporous and at times could not recognize his own family

On admission, the patient was well developed and poorly nourished. The pupils were equal and reacted well. The corneal reflexes were bilaterally diminished, more so on the right. There was weakness of the right external rectus muscle so that the right eye could not be brought beyond the midline on looking to the right. There was ptosis of the left lid and bilateral horizontal nystagmus. The entire right side of the face was paralyzed. The gag reflex was absent, and the patient was barely able to swallow. His speech was dysarthric and somewhat nasal. There was no evidence of weakness of the extremities. Both the finger-to-nose and heel-to-knee tests were poorly executed. The biceps and triceps reflexes and ankle jerks were slightly weak. The abdominal reflex was absent, and there was no ankle clonus. The plantar reflex was absent on the right, and present on the left. There were no other notable abnormalities.

On lumbar puncture, the initial pressure was found to be equivalent to 60 mm of water. The dynamics were delayed, and the final pressure was 0 after the removal of 10 cc. of fluid, which contained 40 lymphocytes per cubic millimeter and 189 mg protein per 100 cc. The gold-sol curve was 0001233210. The Pandy reaction was ++. Examination of the peripheral blood showed no abnormalities.

The patient became progressively worse and more and more stuporous and died 8 months after the first symptoms.

Autopsy. Post-mortem examination showed that the pons, as viewed from the ventral aspect, was unusually broad, the right half being 0.4 cm wider than the left. Horizontal sections disclosed a tumor mass occupying the white matter of the right cerebellar hemisphere, the right middle cerebral peduncle and the tegmentum of the pons and upper medulla on the right side. The tissue there was soft and gray, and was almost liquefied in the central portions. There was no sharp line of demarcation between the tumor tissue and the adjacent brain tissue. In the largest horizontal diameter the lesion measured 3.2 by 3.4 cm. The tumor extended posteriorly to reach the leptomeninges of the cerebellar cortex and medially to the fourth ventricle, which was distorted and almost obliterated by the enlargement of the right cerebellar hemisphere. The lateral and third ventricles were dilated to about twice normal size, and the aqueduct of Sylvius was also enlarged. A slight but definite cerebellar pressure cone had formed. The large arteries showed a slight amount of atherosclerosis. The leptomeninges and dura were not remarkable. The histologic features of the tumor were those of Hodgkin's sarcoma.

It is probable that the right sixth and seventh nerve palsies in this case were due to invasion or compression of the abducens and facial nuclei or of the intramedullary portions of these nerves. Right cerebellar ataxia appeared to be on the basis of destruction of the middle cerebellar peduncle and the right dentate nucleus. The nystagmus was best explained by involvement of the vestibular nuclei. The dysarthria and dysphagia were probably pseudobulbar.

In another case, there was clinical evidence of compression of the spinal cord in both the cervical and dorsal regions. The total protein was markedly elevated, and the gold-sol curve was 000012332. Autopsy showed that masses of tumor tissue had infiltrated between the vertebrae and had surrounded the cord, resulting in marked depression of the fourth through seventh thoracic and the first through third dorsal nerves. In addition, the disease was widespread, involving the muscle of the thoracic wall, the para-aortic lymph nodes, the thalamus, the left cerebral cortex and the liver.

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if indeed they exist, neurologic symptoms may be produced in various ways

In the first place, epidural or subdural granulomatous deposits may surround and press on the cord

Secondly, there may be pressure from lesions arising in the vertebrae or from collapse of vertebral bodies that have been destroyed by the disease. In 92 per cent of Weil's¹⁰ cases, the symptoms could be traced to dural lesions or those in the spine itself. Sudden death has been reported from dislocation of the diseased spine and severance of the cervical cord.¹² In our series, the evidence points to bone lesions as being the most frequent source of cord symptoms

Thirdly, there may be compression or actual invasion of the vessels and lymphatics of the cord by tumor from the adjacent lymph nodes. Weil¹⁰ in particular has stressed this type of involvement. He writes

The mechanism of the myelopathy can easily be explained by the mechanical obstruction of blood vessels and lymphatics supplying the spinal cord through the lympho-granulomatous tissue, either within the intervertebral foramina or outside the spinal canal. It can easily be understood that the interruption or diminution of vascular supply of the spinal cord, if continued over a longer [sic] period of time, will produce a diffuse myelomalacia, which will be the more severe the more spinal arteries are involved

Fourthly, there may be a meningitis.³

And, finally, there may be a toxic myelitis of uncertain nature. Allen and Mercer¹¹ in particular have stressed this origin of the spinal symptoms. Gordon¹³ and others demonstrated that the intracerebral inoculation of rabbits with emulsions of tissue derived from cases of Hodgkin's granuloma produced signs of ataxia, muscular spasms and paralysis. Examination of the cord in such animals reveals few definite lesions. The fact that in experimental animals and in some clinical cases there is a marked disparity between the severity of the clinical manifestations and the paucity of the findings on anatomic or histologic examination raises the interesting speculation whether, in man, certain cases of paralysis may not be due to some ill defined toxin derived from the granulomatous tissue. The possibility cannot be denied, yet extremely careful study at autopsy would be necessary to rule out invasion of the dura or epidural space and lymph nodes pressing on afferent blood vessels. It has recently been demonstrated that the Gordon phenomenon is due to the presence of eosinophils,¹⁴ and in this connection it is worthy of note that in both the cases described by Allen and Mercer¹¹ there was an eosinophilia, amounting in 1 case to 78 per cent.

Nine of our 174 cases, on which we have complete clinical data, showed evidence of paralysis of the legs. In 7, the paralysis was flaccid, in 2, it was spastic. In all 9 cases there was diminution or absence of tactile sensation, and in all there was some disturbance of the rectal and vesical sphincters. In

all, the point of origin appeared to be in the dorsal segments. In Weil's¹⁰ series, the dorsal region was involved in 80 per cent, the cervical in 16 per cent, and the lumbosacral in 4 per cent. Weil regarded paralysis as a late and almost invariably fatal complication. In over 80 per cent of his collected cases the patients died within three months after the appearance of the neurologic symptoms, and none survived more than a year after the onset of the paralysis. That the prognosis is not always so grave is attested by the fact that 3 of our 9 patients survived more than a year after the paresis or paralysis had set in, and 1 was alive and in comparatively good health four years later.

J. C. (HJ 1-30), a 35-year-old policeman, in the early part of 1930 noted enlarged painless lymph nodes in the left side of the neck. A biopsy at that time showed the typical picture of Hodgkin's granuloma. X-ray therapy was instituted, and the nodes promptly subsided. In 1933, the patient developed a mediastinal tumor and a left-sided pleurisy with effusion. Under x-ray treatment and after several chest taps, the mediastinal mass subsided and the fluid disappeared. He remained in fairly good health.

Early in July, 1935, the patient suddenly developed weakness and numbness of both legs. A few days later, he became completely paralyzed from the waist down. There was no pain. He had some difficulty in starting the urinary stream, but no incontinence. The abdominal and cremasteric reflexes were absent. The knee jerks and ankle jerks were equal and hyperactive. There was a bilateral Babinski sign and sustained clonus. No movement could be made from the waist down. Tactile sensation was markedly diminished, and pain sensation was absent below a line parallel with the nipples anteriorly and the midscapular region posteriorly. Lumbar puncture showed evidence of complete block. The initial pressure was equivalent to 160 mm of water. There was no rise on jugular pressure. Coughing or straining caused a rise to 310 mm. The spinal fluid was clear and colorless, with 2 lymphocytes per cubic millimeter. The Pandy test was strongly positive. No gold-sol curve was done.

X-ray studies of the spine revealed no definite abnormalities. There were numerous small, shotty lymph nodes in each side of the neck, each axilla and each groin. The heart appeared to be normal. The left diaphragm was markedly elevated. The abdomen was normal. There was no fever.

High-voltage x-ray therapy was immediately begun over the dorsal spine. Within 3 weeks there was less difficulty in passing urine and tactile sensation began to return. By August 8, approximately 1 month after the onset of the paralysis, the patient was able to move his legs slightly. By the end of August, the improvement was marked, and he was able to move his legs in all directions, though he was unable to bear any weight on them. There were still bilateral Babinski signs and ankle clonus. From that time on, improvement was slow but continued. By June, 1936, a year after the paralysis set in, he was able to walk with crutches, and by October of the same year he could walk without assistance. His general condition was good. Sensation had become normal, and the only abnormal neurologic finding was that both knee jerks and ankle jerks were hyperactive. From July, 1935, to October, 1937, he had received a total of 4300 r (250-kv machine) to the dorsal spine. In September, 1937, he developed a broad band of herpes zoster corresponding to the distribution of the fourth thoracic spinal nerve on the right. After 3 weeks this cleared, leaving a broad scar, as herpes usually does when due to Hodgkin's granuloma.

The patient was able to return to duty as a sergeant in the police force, and although his legs were somewhat weak, he remained active until his death by accident in May, 1939, nearly 3 years after the onset of the paralysis.

No autopsy was performed in this case, and the cause of the symptoms must therefore remain a matter of conjecture. It is probable, however, that

infants The groups are comparable in that most of the infants were delivered between 1910 and 1930. Furthermore, as is shown later in Table 3, the distributions of births according to the ages of the mothers are almost identical for the prediabetic and nondiabetic groups.

The effect of the approaching onset of maternal diabetes on the survival of the fetus is demonstrated by the data in Table 2. The mortality was 15.8

TABLE 2 *The Effect of Approaching Maternal Diabetes on Infant Mortality Rates*

PERIOD OF ONSET OF DIABETES	NO OF BIRTHS	NO OF INFANT DEATHS	INFANT MORTALITY %	
16 or more years	201	12	6.0	6.2*
15 or less years	63	10	15.8	

*Chi square.

per cent among the infants born fifteen years or less before the onset of maternal diabetes. This is a significantly higher mortality than that of 6.0 per cent found for infants born sixteen years or more before the diabetic syndrome was diagnosed in the mothers.

It is a generally recognized fact that the newborn infant mortality increases with the age of the mother. The data in Table 3 show the newborn infant mor-

TABLE 3 *Infant Mortality Rates according to Age of Mother at Time of Delivery*

AGE OF MOTHER yr	NO OF BIRTHS		INFANT MORTALITY %	
	NONDIABETIC	PREDIABETIC	NONDIABETIC	PREDIABETIC
16-20	16	30	0	3.3
21-30	145	146	3.4	5.5
31-40	88	87	0	10.3
41-45	4	4	0	100.0

tality rates according to the age of the mothers at the time of delivery. It is seen that the mortality rates among the infants of nondiabetic and prediabetic mothers are strikingly divergent when delivery occurs in the fourth and fifth decades of life. The absence of any increase in infant deaths in the nondiabetic group as compared with the marked increase in the prediabetic group that occurs in the latter half of the childbearing period suggests that maternal age is a negligible factor in the increasing newborn mortality that occurs as the onset of diabetes is approached in the mothers.

The data on the birth weights of infants born to prediabetic mothers are few, since the chances were small that a woman would enter the New Haven Hospital after the age of forty years with diabetes mellitus and would have been delivered in this hospital several years before. No infants who weighed less than 2500 gm at birth and no twins were included. In Table 4, the average birth weight of 22 infants born to 16 prediabetic mothers is

compared with the average birth weight of infants born to nondiabetic mothers. Determinations for sugar in the urine or for blood-sugar concentrations were made during the course of 20 of the 22 cases.

TABLE 4 *Comparison of Average Birth Weights of Infants of Nondiabetic and Prediabetic Mothers*

STATUS OF MOTHER	NO OF MOTHERS	NO OF INFANTS	AVERAGE BIRTH WEIGHT kg	STANDARD DEVIATION	STANDARD ERROR OF DIFFERENCE
Nondiabetic	40	112	3.53	±0.50	
Prediabetic (total)	16	22	4.15	±0.68	0.16
Prediabetic (15 yr or less before onset of diabetes)	12	17	4.40	±0.55	0.14

Reducing substances were found in the urine of 3 mothers during pregnancy, but in 2 of these the fasting blood sugar was 87 mg per 100 cc in one and 89, 94 and 112 mg in the other. The third mother had three urine examinations made during pregnancy, two of which failed to show the presence of reducing substances. None of the 16 mothers had signs or symptoms of diabetes at the time their infants were delivered. They all subsequently developed diabetes in the fifth or sixth decade of life. Their average age at the onset of diabetes was 45.4 years. Eight of the 16 mothers had passed the menopause before their diabetes became manifest. The 22 infants with but one exception were delivered before the mothers attained the age of forty years. All but 3 of the 22 infants were born six years or more before the onset of maternal diabetes.

The average birth weight of the 22 infants born to 16 prediabetic mothers was 4.15 kg, that of the 17 infants who were born fifteen years or less before the onset of diabetes in their mothers was 4.40 kg. The average weights of both these groups are significantly higher than the average birth weight of 3.53 kg for the nondiabetic group. Three of the 22 infants born to prediabetic mothers weighed more than 5.0 kg at birth, 6 weighed over 4.5 kg and 15 weighed 4.0 kg or more. These incidences are approximately two hundred, twenty-seven and seven times greater than the expected ratio of births in these respective weight categories.^{3,4}

Ten of the 16 mothers in the prediabetic group reported in Table 4 attained a weight of 175 pounds either during the childbearing period or subsequent to it. Because obesity is one of the frequent characteristics of women developing diabetes in later life, and because it seemed possible that the maternal obesity was a factor in the increased birth weights, a study was made of the birth weights of infants born to women who were obese at the time of pregnancy (Table 5). No significant difference was found between the average birth weight of the infants in the obese group and those in the non-diabetic group.

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THE EFFECT OF THE PREDIABETIC STATE ON THE SURVIVAL OF THE FETUS AND THE BIRTH WEIGHT OF THE NEWBORN INFANT*

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ONE of the outstanding characteristics of infants born to diabetic mothers is a high fetal and neonatal mortality rate. In addition there occur in some infants born to diabetic mothers striking somatic and visceral changes, among which are an increased birth weight, cardiomegaly, hyperplasia of the islands of Langerhans, excessive extramedullary erythropoiesis, hyperplasia of the adrenal glands and an increase in the eosinophil elements of the anterior pituitary body.¹ Similar observations have been made on infants born to mothers who were not diabetic at the time of delivery but in later months or years developed signs and symptoms of diabetes.² Since all the mothers who have been studied thus far became diabetic during the childbearing period,—that is, under forty years of age,—it was considered desirable to extend the observations to infants born to mothers whose diabetes appeared after they had passed the fourth decade.

SOURCE OF DATA

The files of the New Haven Hospital were searched for records of women who developed diabetes after forty years of age. The time of onset was determined by the history of the appearance of the first symptom or the detection of glycosuria and hyperglycemia. A history of a birth was acceptable only in case the age of the mother at the time of the birth of the infant and all its siblings could be determined. Infant deaths in this study include all cases listed as stillbirths and all infants dying in the first week of life. A birth weight was considered acceptable only in infants born in the New Haven Hospital. A control group of infant cases was obtained from the records of women admitted to the New Haven

Hospital after the age of forty with diagnoses other than diabetes mellitus. Histories of births and birth weights in the control group were subjected to the same restrictions as were imposed on the diabetic group. A third group of infants born to obese but nondiabetic mothers was also studied in respect to their birth weights. The diagnosis of obesity was limited to women weighing two hundred pounds or more during a pregnancy or one hundred and seventy-five pounds or more when not pregnant but while still in the childbearing period.

RESULTS

The mortality rate for infants born to mothers who subsequently became diabetic during or after the fifth decade of life has been compared to the rate among infants of nondiabetic mothers (Table 1). The mortality rate of 8.3 per cent for the pre-

TABLE 1 The Mortality Rates among Infants Born to Nondiabetic and Prediabetic Mothers

STATUS OF MOTHER	NO OF MOTHERS	NO OF BIRTHS	NO OF INFANT DEATHS	MORTALITY RATE %	
Nondiabetic	59	253	5	2.0	10.5*
Prediabetic	57	264	22	8.3	

*Chi square

diabetic group is significantly higher than that of 2.0 per cent for the nondiabetic group. It is not supposed that the mortality rates are exact for either group of infants, since, in a history, deaths of infants are likelier to be overlooked than are surviving infants and some so-called "miscarriages" may have been prematurely born infants who failed to survive. It is believed, however, that any errors involved in obtaining true infant mortality rates from histories recorded several years later are equally distributed between the two groups of

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MEDICAL PROGRESS

THE PARENTERAL USE OF VITAMIN PREPARATIONS*

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IN 1943 the National Research Council¹ published what it considered to be adequate daily allowances of the better known vitamins. Although the recommended amounts have been attacked as too large from the viewpoint of minimum requirements, these allowances, which admittedly include a factor of safety of at least 30 per cent,² provide physicians with standards concerning the vitamins a normal person should ingest. The field of parenteral vitamin therapy, by contrast, appears to be one of hopeless confusion. Parenteral vitamin preparations of all types are, literally and figuratively, a drug on the market, but information concerning their proper use is indeed scarce. What vitamins should be given parenterally? How much vitamin is lost in the urine after an intravenous injection? What are the needs of the patient who is ill enough to require parenteral administration of vitamins? In this review, an attempt is made to answer some of these questions in the hope of making available some guiding principles to the physician who is at times forced to resort to parenteral vitamin therapy. Because the available evidence is limited, and often indirect or equivocal, conclusions reached and dosages suggested must at best be considered roughly approximate and highly tentative. Emphasis in this discussion is placed on the needs of the average medical or surgical patient whose nutrition must be maintained but who, for some reason or other, requires the parenteral administration of vitamins. No attempt is made to discuss the treatment of specific and advanced deficiency diseases, such as pellagra, scurvy and so forth.

Vitamins, like other foodstuffs, are best taken by mouth. Parenteral administration is, however, justified for certain patients, who include the following: those unable or forbidden to take any food by mouth, those suffering from a defect in intestinal absorption, those who are so acutely deficient in vitamins that the delay of intestinal absorption must be circumvented, those who require fairly large doses of vitamins but suffer from a disorder that oral preparations might aggravate (a physician might prefer, for example, to treat a patient with ulcerative colitis with parenteral vitamin B complex rather than to give large doses of brewer's yeast by mouth), and those unable or unwilling to ingest a specific vitamin preparation that is indicated.

The kind and amount of vitamins needed by patients in the above categories naturally vary from case to case, for some of the patients will be able to eat and absorb at least a part of their vitamin requirements. The dosages suggested in this review, however, are intended for the patient whose total needs for the vitamin under discussion must be supplied by parenteral means. In computing these needs, one must allow for the daily requirement as well as the amount necessary to build up vitamin stores depleted by illness or deficient diet. Except when laboratory facilities are available for testing a patient's vitamin reserve, the amount of vitamin needed to replenish his stores must be estimated. For any one vitamin, this amount presumably lies somewhere between the normal requirements and the needs of a patient frankly deficient in that particular vitamin. It might be argued that vitamins are safe. Why not give huge doses and be sure that the patient's needs are covered? Besides the expense involved in such a practice, it is difficult to justify nonspecific and grossly excessive vitamin therapy merely on the grounds that vitamins are relatively nontoxic substances.

In estimating the vitamins needed by any patient, his whole nutrition should be considered as a unit. One cannot consider the vitamin and the caloric intakes independently, nor does intensive therapy with a single vitamin appear to be judicious in the average case. The interrelation of vitamin needs and caloric intake is illustrated by the person who is subjected to complete starvation. He is not liable to develop an acute vitamin deficiency. Should he, however, terminate a prolonged fast by ingesting large quantities of sugar, symptoms and signs of various deficiencies might develop in rapid order. The reason for this sequence of events is that vitamins take an active part in metabolic processes. In starvation, metabolism is depressed, relatively few calories are burnt up, and the need for vitamins is correspondingly reduced. When calories are supplied to the body by sugar, however, the depleted vitamin stores are rapidly consumed, and frank manifestations of deficiency appear. In view of these facts, the patient who has had a calorically deficient intake may have better vitamin stores than the one who has taken a calorically adequate but vitamin-poor diet. Similarly, a man subsisting on parenteral nutrition is more in need of vitamins if his caloric intake is adequate than if it is deficient. Obviously, one should aim in such a case at an

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COMMENT

The nature of the factor or factors responsible for the increased newborn mortality and increased birth weights of infants born to prediabetic mothers remains unknown. Presumably the primary factors

TABLE 5 Comparison of Average Birth Weights of Infants of Nondiabetic Mothers and Obese Mothers

STATUS OF MOTHER	NO OF MOTHERS	NO OF INFANTS	AVERAGE BIRTH WEIGHT kg	STANDARD DEVIATION
Obese	17	21	3.60	± 0.54
Nondiabetic	40	112	3.53	± 0.50

are the same as those that are responsible for the high mortality and increased birth weight of infants born to mothers who already have developed diabetes. Recent studies by Smith, Smith and Hurwitz⁵ suggest that fetal and neonatal deaths in diabetic pregnancies are related to a premature increase in estrogen and progesterin production by the placenta, followed by a decreased production of these same steroids at an earlier time in the gestation period than is to be expected. White and Hunt⁶ have urged the treatment of diabetic pregnant mothers with estrogen and progesterone on the basis of an observed imbalance of the sex hormones in pregnancies terminating fatally for the fetus or newborn infant. The striking changes in the islands of Langerhans, adrenal glands, gonads and anterior hypophysis of some infants born to diabetic mothers are additional evidence that endocrine factors are almost certainly involved in their production. The fact that all these dramatic changes can be found in the infant several years before there is any evidence of diabetes in the mother² suggests that additional knowledge of the etiology of diabetes is to be gained by further study of the factors responsible for the increased mortality rate and the somatic and visceral changes seen in infants born to diabetic mothers.

The causes of death in many fetuses and newborn infants are still unexplained or poorly understood. The results of the present study indicate that a certain percentage of these deaths are now to be accounted for on the basis of factors associated

with the subsequent development of diabetes in the mothers. The fact that fetal and neonatal deaths are increased for several years before the appearance of diabetes in the mothers points toward a high degree of sensitivity on the part of the human fetus to the factors involved, whether or not they are endocrine.

The data presented in this study indicate a new explanation for the excessive birth weight of some fetuses. The number of infants weighing over 4 kg at birth whose excessive birth weight can be accounted for on the basis of a prediabetic state cannot be judged from the few cases reported here. The fact that 11 of the 12 mothers who had babies born to them fifteen years or less before the onset of maternal diabetes were delivered of infants weighing 4 kg or more suggests that women developing diabetes past the childbearing period are recruited almost wholly from 5 to 7 per cent of mothers who give birth to babies weighing over 4 kg.

CONCLUSIONS

The fetal and neonatal mortality rates and the average birth weight are increased among infants born to mothers who subsequently manifest diabetes mellitus, even though the latter do not develop the disease until after forty years of age.

The fetal and neonatal mortality rates increase as the onset of maternal diabetes is approached.

Maternal obesity is not a factor in the increased average birth weight of infants born to prediabetic mothers who become diabetic after the age of forty.

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certain issue, the thiamine excreted in the urine is not necessarily the amount "left over" after metabolic and storage needs are satisfied. Nevertheless, a considerable body of opinion^{6, 21} claims that the urinary excretion of vitamin B₁, after a specific test dose is given, is a good index of a patient's nutrition with respect to thiamine chloride. This appears to be particularly true if small test doses are given. A deficient subject, for example, has been found to excrete 2 to 6 per cent of a subcutaneous dose of 1 mg of vitamin B₁ within twenty-four hours, whereas a subject with good stores excretes over 20 and often 50 per cent of such a test dose.^{27, 28} Urine collected for a four-hour period after a subcutaneous dose contains most of the thiamine excreted in response to the injection, hence, after 1 mg of vitamin B₁ subcutaneously, the four-hour urine in deficient subjects contains about 30 to 70 microgm, in normal subjects about 200 microgm, and in saturated subjects 500 to 700 microgm.^{29, 30} These figures do not differ greatly from the average results obtained after oral or intravenous dosage. Three hours after an oral dose of 1 mg, about 65 microgm is excreted by deficient and about 200 microgm by saturated subjects.²⁴ An intravenous dose of 1 mg of thiamine chloride in normal subjects is followed by an excretion of 100 to 200 microgm in the first half hour, but the four-hour total is again in the vicinity of 15 to 25 per cent of the test dose.^{31, 17}

Although oral test doses of 5 mg of vitamin B₁ have been used,^{18, 30} the parenteral administration of such a large dose has not found much favor as a diagnostic test for thiamine deficiency on the grounds that large doses "flood" the blood stream and are excreted by the kidney irrespective of the subject's needs, thus masking the difference between normal and deficient subjects.^{19, 31, 32} In one series, an oral test dose of 5 mg led to the excretion of 13 per cent in twenty-four hours in normal subjects, but 25 per cent of a similar intravenous dose appeared in the urine within four hours, and an intravenous injection of 30 mg led to a 50 per cent excretion.³¹ In deficient subjects, 12 per cent of an intravenous dose of 5 mg and 40 per cent of an intravenous dose of 30 mg were found in the four-hour urine samples. According to Borson,¹⁹ the loss of thiamine in the urine following an intravenous injection of the vitamin occurs chiefly during the first hour and is of the following order of magnitude

intravenously. If the vitamin is given subcutaneously in large doses, its excretion in the urine during a three-hour period may be roughly similar to the findings after intravenous injection. 10 mg of thiamine given subcutaneously is followed by a 20 per cent excretion, and 50 mg by a 26 per cent excretion.³³

Although the urinary output of thiamine after an intravenous dose may occasionally be small (only 2.8 per cent one hour after 15 mg intravenously¹⁸), it seems fair to conclude that the parenteral administration of thiamine in doses over 3 mg may be attended by an apparent urinary loss of 15 to 30 per cent, with increasing percentages attending higher doses. This loss, however, tends to be near the lower end of the range in deficient patients and probably far above 30 per cent in those who are saturated.

It is theoretically possible that the urinary excretion of thiamine is slightly less after subcutaneous administration or after a slow intravenous infusion than after an intravenous dose given during the course of half a minute. Caution must, however, be exercised in estimating the effectiveness of adding thiamine to an intravenous infusion. Early in his studies with the fractions of the vitamin B complex, Cowgill³⁴ showed that these substances can be washed out by diuresis. It was subsequently shown that the diuresis that attends thyrotoxicosis may carry with it considerable quantities of thiamine, even though the blood level of vitamin B₁ is low in this disease.^{16, 19} When a mercurial diuretic is given, the ensuing diuresis may increase the excretion of injected thiamine to 60 per cent of the dose given.¹² The fact that diuresis can affect thiamine excretion profoundly has led to the suggestion that this vitamin is a nonthreshold substance,¹⁹ and a renal-clearance study indicates that an extensive tubular resorption of thiamine does not take place.¹⁴ Consequently, if an intravenous infusion is of such a composition, or if it is given at such a rate that diuresis is evoked, an increased amount of any thiamine given with the infusion is presumably lost in the urine.

Requirements. Estimates of the minimum requirement of thiamine for the normal adult person vary from 0.2²² to 0.6 mg per 1000 calories.²⁹ No benefit, however, is said to obtain from ingesting more than 1 mg for each 1000 calories of food.²³ If one is guided by the more generous estimates of the needs of a normal man, a patient who receives 1500 calories per day, whether by mouth or by vein, should get about 1 mg of vitamin B₁ daily. His disease, however, may or may not alter the thiamine requirements. In exercise, which may be comparable to disease in that the metabolic rate is elevated, the vitamin B₁ needs rise with the caloric requirements, but apparently the requirement of thiamine per calorie is not increased.²² It is also stated that the evidence for an increased require-

DOSE OF THIAMINE mg	URINARY EXCRETION %
3	15
7	20
10	30
30	50
50	80

Gorham et al¹² recovered between 411 and 1530 microgm in the twenty-four-hour urine of normal subjects after 5 mg of vitamin B₁ had been given

adequate supply of calories fortified with the necessary vitamins

The necessity of a balanced vitamin therapy, particularly with respect to the vitamin B complex, is still a matter of debate. Yet it seems likely that a patient who is receiving all his nutrition parenterally requires not only thiamine chloride but also other fractions of the vitamin B complex, unless good evidence is available that the stores of these other fractions are adequate. As a matter of fact, the clinical impression is strong that the intensive administration of a single component of the vitamin B complex to a patient whose stores of vitamin B complex are low accentuates the needs for the other fractions.⁵⁻⁶ Animal experiments both confirm^{7, 8} and negate⁹ the clinical impression that intensive therapy with a single vitamin may be harmful. By far the greater part of the evidence indicates, however, that parenteral vitamin injections that are given for the purpose of maintaining nutrition should never consist of a single vitamin. Only in case a specific indication for treatment with a single vitamin exists — the vitamin K deficiency of obstructive jaundice, for example — does it seem warranted to inject one particular vitamin.

Methods for the quantitation of vitamins in the tissues, body fluids and excreta of man vary tremendously, both in reliability and in technic. Not infrequently the results obtained from bioassay and chemical analysis do not coincide. Consequently, values for vitamin concentrations reproduced in this text from the literature are subject to change when more specific methods are developed, although the figures given for such well studied vitamins as thiamine chloride and ascorbic acid show quite satisfactory correlation irrespective of the method of determination.

For purposes of clarity, two terms that are used throughout this review, "saturation" and "biosynthesis," should be defined.

Saturation In searching for a laboratory test of vitamin deficiency, investigators have administered a vitamin in specific amounts — the "load" — and have then determined the quantity of that vitamin excreted in the urine during a certain time period. According to the theory behind this test, a deficient subject excretes only a minute fraction of the test dose. As treatment with the appropriate vitamin is given, the subject excretes a gradually increasing proportion of the test dose until the amount excreted reaches a limit beyond which it will not rise, even though the subject continues to receive intensive vitamin therapy. At this point, he is considered to be saturated, that is, his body is considered to have stored as much of the vitamin as it can possibly hold, and any extra vitamin given is in large part destroyed or excreted in the urine. There is no evidence that a patient has to be

saturated before his vitamin stores can be considered optimum, a much smaller quantity probably suffices for normal function.¹⁰

Biosynthesis Certain organisms in the intestinal tract of animals and man, particularly the coliform bacteria,¹¹ can synthesize various vitamins. This process is referred to as intestinal biosynthesis.

THIAMINE CHLORIDE

Thiamine chloride (vitamin B₁) is a water-soluble substance that is present in the blood both as free thiamine and as a phosphorylated compound, diphosphothiamine. The latter, also known as cocarboxylase, appears to be the physiologically active form of vitamin B₁,¹² and is found in tissues and the cellular elements of the blood.¹³ Free thiamine, which constitutes a small fraction of the blood's total thiamine content, is chiefly present in plasma.^{13, 14} The average blood values¹²⁻¹⁷ are as follows:

Total thiamine	4-10 microgm. per 100 cc. whole blood
Diphosphothiamine (chiefly in white cells and red cells)	3-9 microgm. per 100 cc. whole blood
Free thiamine (chiefly in plasma)	0.5-2.0 microgm. per 100 cc. plasma

The concentration of thiamine in the tissues of the human body is about ten to twenty times that of whole blood, the total vitamin B₁ content of a normal man averaging about 25 mg.^{5, 18} When illness and poor nutrition beset a patient, the tissue stores of thiamine may be drastically reduced.¹

Solutions containing pure thiamine are suitable for subcutaneous or intravenous injection. When so given, the vitamin is apparently phosphorylated rapidly in such organs as the liver and the kidneys.^{12, 19} and is in part used in metabolic processes. Some is stored in the tissues, some is excreted in the urine, and insignificant amounts are lost in the feces and sweat.^{12, 20-23} Actually, the absolute amount that can be measured as having been stored in the tissues is extremely small and limited.^{12, 18, 20, 24} and the amount lost in the urine may be but a small fraction of the dose given, even if some possible metabolites of vitamin B₁ are taken into account.¹² It follows that considerable thiamine undergoes processes of metabolism or destruction that cannot be followed at present. Some light is shed on this problem, however, by studies using thiamine tagged with radioactive sulfur.²⁵ When such thiamine is given intramuscularly for four days to a human subject, 61 per cent of the tagged vitamin is recovered from the urine and 11 per cent from the feces in the ten days following the first injection. These studies also show that a sizable proportion of the thiamine excreted in the urine after vitamin B₁ is given parenterally is not derived from the injected dose but apparently is stored thiamine that is displaced from the body when more vitamin B₁ is administered.

Since the metabolism of vitamin B₁, particularly the question of destruction in the body,²⁶ is an un-

doses of thiamine constitutes another argument against injecting vitamin B₁ in amounts far in excess of what is needed for adequate nutrition

Biosynthesis of thiamine chloride apparently occurs in the human intestine,^{20, 49} but its implication in human nutrition is debatable.^{40, 50} The fact that 50 mg of thiamine given by retention enema increases the urinary excretion of the vitamin has been advanced as evidence that the vitamin B₁ biosynthesized in the human colon is available for man's nutritive needs.⁴⁰ This evidence has been attacked on the grounds that 50 mg is far in excess of the amount usually produced in the intestine (the average fecal vitamin B₁ content in man is 150 to 350 microgm per day⁴⁹) and that most of the thiamine in the feces is present as unabsorbable cocarboxylase.⁵⁰ In view of the well known tendency of enemas to regurgitate into the ileum, it is also questionable whether absorption after a retention enema proves that this occurred in the large bowel. From the viewpoint of the patient who requires parenteral nourishment, however, the debate is somewhat academic. Intestinal disease per se may affect biosynthesis in an unknown manner. If, as is likely, the patient is not able to eat, his gut lacks the fiber and starches that appear to stimulate thiamine production by the intestinal organisms.⁴⁹ Finally, many of the patients receiving vitamins parenterally may have received or are receiving sulfonamides, which depress the organisms chiefly responsible for biosynthesis.^{11, 40, 51} It seems that the vagaries of disease, the cessation of oral feeding and the intestinal disinfectants used before and with surgery tend to eliminate intestinal biosynthesis as an important factor in maintaining the necessary supply of thiamine.

RIBOFLAVIN

Riboflavin is a water-soluble fraction of the vitamin B complex. In human blood, it is chiefly present in the red cells, in concentrations ranging between 35 and 50 microgm per 100 cc of whole blood.^{52, 53} In human tissues, between 2 and 13 microgm of riboflavin are present per gram of tissue.^{3, 52} Man's bodily stores of riboflavin thus appear to be about four to six times his thiamine stores, a ratio that also holds true in the rat.⁵⁴

Like other pure fractions of the vitamin B complex, solutions containing pure riboflavin can be injected subcutaneously or intravenously. The intravenous route was used by Axelrod et al.⁵⁴ in carrying out a series of saturation tests with 200 microgm of riboflavin per kilogram (10 mg riboflavin for a subject weighing 110 pounds). In the twenty-four hours subsequent to the injection, 10 to 63 per cent of the test dose was recovered from the urine, the response of normal subjects apparently not differing from that of patients presumably deficient in riboflavin. With a larger dose — 400

microgm per kilogram — 72 per cent was excreted in the urine during the first twenty-four hours. These results led Axelrod and his collaborators to decide that the saturation test was not useful in diagnosing riboflavin deficiency. Subsequently, however, it was shown that test doses employing 1 mg intravenously,^{3, 55} 2 mg subcutaneously⁵⁶ or 16 microgm per kilogram (a total of about 1 mg) intramuscularly⁵⁷ led to urinary excretions that showed good correlation with the subject's nutritional status. The deficient subjects, in general, excreted below 25 per cent of the test dose in the four hours immediately following the injection, the excretion of normal subjects varied between 25 and 75 per cent, whereas saturated individuals excreted 70 to 100 per cent. No difference was apparent between oral and intramuscular test doses when a small dose (16 micrograms per kilogram) was used.⁵⁷ The difference between the results of Axelrod et al. and those of the other investigators has been ascribed to the large parenteral doses used by the former.^{55, 58} Riboflavin, like thiamine, is apparently retained according to the needs of the patient when given in small parenteral doses, but when larger doses (5 mg or more) are injected, the urinary loss is also affected by renal function, by the extent to which the blood stream is loaded and by other variable factors.

Requirement. Keys,⁵⁸ in 1944, wrote that the "estimation of the riboflavin requirement of man and the diagnosis of riboflavin deficiency are in a peculiarly unsatisfactory state." The truth of this statement can be appreciated when one realizes that some nutritional surveys continue to accept cheilosis and corneal vascularization as specific evidences of riboflavin deficiency, although careful studies⁵⁵⁻⁶⁰ suggest that such a view is incorrect.^{61, 62} Since the signs of riboflavin deficiency are the object of debate, the daily requirements are also uncertain. The National Research Council¹ proposed 2.7 mg for a moderately active adult male of 70 kilograms (0.9 mg per 1000 calories). On the other hand, a diet offering only 0.31 mg of riboflavin per 1000 calories produced no physiologic handicaps, although it may have lowered the body's reserves of the vitamin.⁵⁸ Others believe that the minimum requirement to maintain adequate stores is above 0.5 mg of riboflavin per 1000 calories.⁵⁶ The allowance for an ill patient might therefore be placed at 1 mg per 1000 calories. On this basis, a daily parenteral dose of 3 to 4 mg would both satisfy a patient's daily needs and allow for a 25 to 30 per cent loss in the urine.

The body's stores of riboflavin appear to be less rapidly depleted than those of thiamine. All the tissues of 3 chronically ill patients studied by Ferrebee and Weissman³ were found to contain extremely low levels of vitamin B₁, but the riboflavin levels were below normal in only 1 case, a tuber-

ment of thiamine in fever is at present not conclusive.³⁵ In dogs, dinitrophenol raises the basal metabolic rate and produces some fever, but apparently does not increase the need for vitamin B complex.³⁶ On the other hand, thyrotoxicosis may increase the daily requirement two and a half times,^{37, 38} and a daily dose of 10 to 20 mg of vitamin B₁ is recommended in this disease.¹⁶ This increased requirement in hyperthyroidism is probably due to an increased caloric consumption, to diuresis, to unknown factors and perhaps to hepatic dysfunction, which may cause the phosphorylation of vitamin B₁ to be impaired.^{15, 39} It is probably safest to consider that the needs for thiamine are increased in disease,²² and that a requirement of 1 mg per 1000 calories be arbitrarily chosen. Allowing for a 25 per cent loss in the urine, a patient unable to ingest food but presumably with normal stores of thiamine—a case of acute appendicitis and peritonitis, for example—should therefore receive 3 mg of parenteral vitamin B₁ a day if he is given about 2000 calories a day by means of intravenous infusions.

Unfortunately most patients who require parenteral administration of thiamine do not have normal stores of this vitamin. Of all the vitamins, the body seems to have least capacity to store thiamine chloride, evidences of deficiency at times appearing within a few days after a nonsaturated normal subject has taken a thiamine-free diet.²³ Longer intervals, ranging between twenty and forty days, are usually necessary, however, before a normal subject on a thiamine-free diet develops severely depleted stores²⁵ or unequivocal signs of deficiency.^{22, 40} Even saturation by means of excessive doses of vitamin B₁ will not ensure storage for more than two or three weeks.^{24, 27, 31} Patients, of course, do not subsist on a thiamine-free diet, but the quantity of vitamin B₁ actually available to their metabolic needs is often limited for a variety of reasons. Sometimes the nature of the illness causes the patient to consume a diet limited in its content of the vitamin B complex, although the caloric intake is adequate by dint of taking bland, starch foods. Or the patient may have consumed adequate quantities of thiamine, but its absorption may have been impeded by gastric anacidity, excessive intake of antacids or a diarrheal state of some type.^{41, 42} Finally, as has been mentioned, fever, hyperthyroidism, renal function or hepatic function frequently influences the patient's metabolism and storage of vitamin B₁.

Unless facilities are available for measuring the thiamine content of the urine, the estimation of a patient's thiamine stores is practically impossible. A probable range, however, can be proposed. In a subject on a thiamine-deficient diet for twenty days, an oral dose of 5 mg of vitamin B₁ daily for six days was necessary before a normal response

to a saturation test was observed.¹⁸ A patient with a low thiamine excretion in the urine following a saturation test responded normally after 10 mg of vitamin B₁ had been given daily for five days.¹ In another study, roughly 15 mg by mouth daily for ten days was apparently not quite enough to correct the biochemical abnormalities in a severely depleted subject.²⁹ A total dose of 100 to 125 mg was necessary to saturate deficient patients with alcoholic neuritis, but this dosage may have exceeded the total deficit, since liver function was obviously affected in these subjects.¹⁹ Spies⁴³ recommends 25 mg daily for patients with beriberi. In thyrotoxic patients, 10 mg of vitamin B₁ given parenterally twice daily for six to ten days elevated the thiamine content of the blood to normal levels.¹⁶ These figures for the needs of subjects with definite thiamine deficiency, taken in conjunction with the fact that the total vitamin B₁ content of man averages 25 mg,¹⁸ suggest that the patient who has no clinical signs of thiamine deficiency but whose stores have presumably been depleted during his illness needs about 50 mg of thiamine in addition to his daily requirements. For patients who have to receive this supplement parenterally, 10 mg a day for ten days should suffice to cover daily needs, repletion of stores and urinary losses. After ten days, the dosage can be decreased to the amount estimated as the daily requirement.

In many patients, the suggested dosages will probably be excessive, in others, particularly, if thyrotoxicosis, fever or diuresis complicates the picture, they may be insufficient. There seems to be little indication, however, for injecting huge doses of thiamine chloride unless frank and acute symptoms of deficiency are present. Repeated doses of 100 mg daily, for example, presumably lead to a large urinary loss, which, if the patient is saturated, may approximate the dose injected. To be sure, it has been suggested that the metabolic exchanges in which thiamine participates are impaired under certain conditions, such as shock, anoxia and irradiation sickness,^{44, 45} and that large doses of vitamin B complex may in part correct the abnormality. The efficacy of large parenteral doses of thiamine, niacinamide or pyridoxin in irradiation sickness or analogous disorders remains, however, to be proved. It seems advisable, when possible, to ensure proper nutrition before starting radiation therapy.⁴⁶

One rare complication of parenteral thiamine therapy is sensitization to the vitamin. In the reported cases,^{47, 48} the following train of events is usual: repeated and large doses of vitamin B₁ are injected into a patient, a period without therapy follows during which sensitivity presumably develops, resumption of parenteral thiamine therapy is thereupon followed by acute allergic symptoms, which may include respiratory distress and collapse. The fact that many of these patients received huge

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culous patient who had been maintained on parenteral glucose and saline infusions for two weeks. Normal subjects, whose stores had been well supplied, consumed a diet restricted in riboflavin for thirty days before the urinary excretion after a saturation test was significantly decreased.^{66, 68} Conversely, in markedly deficient subjects, a total riboflavin dosage of 40 to 50 mg, given daily in small oral doses, was sufficient to bring about saturation as judged from the fact that the daily urinary excretions of the vitamin attained a constant, high plateau.⁶⁸ Eleven milligrams of riboflavin daily for a week appeared to be more than enough to "supercharge" subjects who had had no clinical evidence of riboflavin deficiency but who had subsisted on a restricted regimen (0.31 mg riboflavin per 1000 calories) for five months.⁶⁸ From these figures, it appears that a patient who has been ill or who has had a restricted riboflavin intake for less than two weeks requires no more riboflavin parenterally than that given to cover his daily requirement. For patients who have been subjected to possible riboflavin deprivation for longer periods, 10 mg for five days should compensate for any depleted stores that may exist, unless the metabolism of riboflavin is radically altered by disease.

The interrelation of riboflavin with other food-stuffs is of some theoretical importance. On the basis of animal experiments, it has been suggested that the absorption and utilization of riboflavin is impaired in thiamine deficiency.⁶⁴ In man, such a relation is not demonstrable, and the explanation has been offered that the apparent interrelation between vitamin B₁ and riboflavin may be a non-specific phenomenon when tissues are broken down and weight is lost (due to thiamine deficiency, in this case), riboflavin is liberated and excreted as an unused product of tissue catabolism.⁶⁴ In line with this suggestion is the fact that riboflavin excretion in laboratory animals and in man is increased during periods of protein depletion or starvation.⁶⁶ After periods of protein depletion, the hepatic stores of riboflavin are decreased, with adequate protein supplies, the hepatic riboflavin content is increased.⁶⁶ Hence, in animals, protein deposition in the liver appears to be necessary to retain riboflavin in this organ, which is a major site of riboflavin storage in man (liver tissue contains 13 microgm of riboflavin per gram⁸⁷). The administration of adequate amino acids⁶⁷ to a patient requiring parenteral nourishment may therefore promote the storage of any riboflavin that is given.

Small injections of thiamine chloride may temporarily increase the urinary output of riboflavin in normal human subjects, but this observation seems to be of little nutritional significance since large doses of vitamin B₁ given for one to ten weeks do not produce any clinical or biochemical evidence of riboflavin lack.⁶⁸

The biosynthesis of riboflavin appears to occur in man.⁶⁹ Although succinylsulfathiazole does not decrease the fecal riboflavin output,⁶⁹ the small amounts of riboflavin produced, the question of their availability⁷⁰ and the unpredictable effects of disease on intestinal biosynthesis argue that one should not rely on this source in estimating a patient's riboflavin needs.

(To be concluded)

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rate of 50, and the sounds were of fair quality, with a harsh systolic murmur in the aortic area. The left lower extremity was white and paralyzed, with no sensation or reflexes. Neither femoral pulse could be palpated.

The blood pressure was 120 systolic, 60 diastolic on the right, and 130 systolic, 60 diastolic on the left.

Shortly after arrival at the hospital the patient gasped and expired within a few minutes.

DIFFERENTIAL DIAGNOSIS

DR. PAUL D. WHITE: This patient showed evidence of intracranial bleeding. Subarachnoid hemorrhage could have explained the situation, and I was going to ask Dr. Kubik, if he were here, about the various etiologic factors in the production of an intracranial aneurysm that might rupture and produce such symptoms, perhaps Dr. Castleman can answer the question. Bleeding from the ordinary congenital aneurysm in the circle of Willis, with which we have of late become somewhat familiar, has in my experience given rise oftener to headache than to pain in the back of the neck. Here we have a sixty-three-year old man with evidence of syphilis. Can syphilis cause an aneurysm of the circle of Willis, such as we see in young persons with congenital weakness of the vascular wall? Since this man probably had central-nervous-system syphilis, which is essentially vascular syphilis, there need not have been an actual aneurysm but rather a diffuse involvement of the blood vessels of the meninges, a kind of internal hemorrhagic pachymeningitis, of which one of the causes is syphilis. I believe that is likelier than rupture of an aneurysm, especially in view of the fact that the symptoms continued in somewhat the same fashion in later periods. I speak of this now because I shall leave this part of the picture shortly, becoming involved with other lesions.

At the second hospital admission there was evidence of the beginning of what, from the sequence of events, probably was involvement of the heart in the syphilitic process, namely, the development of slight aortic regurgitation. The diastolic murmur in the tricuspid area was undoubtedly an aortic diastolic murmur, heard at the lower end of the sternum much better than over the aortic area, which is not infrequently our experience. Therefore we may suspect that this is evidence of aortitis, which had been there long before but had not previously involved the aortic ring. Whether all these attacks of headaches and soreness and other nervous disturbances were due to intracranial hemorrhages or thromboses it is difficult to say, but I think that they fit into the diagnosis of pachymeningitis, such as I have mentioned.

I want to interpolate between the second and third hospital admissions the question whether there is any record of antisyphilitic therapy. There is no mention of it here. That might have been a serious

omission in therapy because of the evidence, in both the central nervous system and the cardiovascular system, that syphilis was there and should have been treated. It is in the early stages that one can sometimes stop the progress of aortitis.

DR. BENJAMIN CASTLEMAN: He was given five doses of bismuth subsalicylate between the second and third admissions.

DR. REED HARWOOD: The physician who took care of him at that time decided not to continue the treatment, I do not know why.

DR. WHITE: Then the treatment was inadequate. There was progression of the cardiac involvement, and the onset of left ventricular failure, owing to the development of free aortic regurgitation.

Have we any x-ray films?

DR. MILFORD D. SCHULZ: Apparently the films were lost except for one oblique view. There seems to be definite enlargement of the left ventricle.

DR. WHITE: Can you see the aorta?

DR. SCHULZ: This is a left antero-oblique projection but the aortic shadow cannot be accurately traced.

DR. WHITE: The electrocardiogram is characteristic of the left ventricular strain that is found with aortic regurgitation. There is also an effect from digitalis, as shown by sagging of the ST segments. This may be a combined effect involving both.

Death occurred two years after the discovery of the cardiac involvement, this is a common duration of life following the diagnosis of cardiovascular syphilis in inadequately treated cases. It is difficult to tell whether nitroglycerin given earlier would have been strikingly helpful. The story sounds like one of prolonged attacks of angina pectoris coming at rest. The chief symptom is characteristic of angina pectoris, but it is of longer duration than usual. Its atypical character is quite in keeping not only with a slowly developing early arteriosclerotic coronary occlusion but also with aortitis with occlusion of the mouths of the coronary arteries.

I do not know the significance of the epigastric tenderness. I wonder if it was marked. Do you recall, Dr. Harwood?

DR. HARWOOD: It was moderate.

DR. WHITE: This was probably due to gastric irritation. Was there an electrocardiogram taken during the period of the last few days before the final hospital admission?

DR. HARWOOD: No.

DR. WHITE: There was probably no time for an electrocardiogram to have been taken when he came into the hospital because he lived only a few minutes.

DR. HARWOOD: One was taken fifteen minutes before he died.

DR. WHITE: I should like to see it shortly.

This terminal complication is, of course, one of the chief problems of interest. The diastolic murmur

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 31391

PRESENTATION OF CASE

First admission A sixty-three-year-old man was admitted to the hospital complaining of severe headache.

For a number of years he had had episodes of weakness and vertigo, without loss of consciousness. An hour before admission he complained of pain in the back of the neck. Fifteen minutes later he was found unconscious and breathing heavily. In forty-five minutes he regained consciousness and on admission complained of suboccipital and neck pain.

Six months before admission the patient had undergone a perineal prostatectomy and recovered uneventfully. At that time the blood pressure was 130 systolic, 70 diastolic, and no cardiac murmurs were heard.

On physical examination the neck was stiff. The pupils reacted to light and accommodation. The tendon reflexes were more marked on the right than on the left. The plantar responses were normal. There was no disturbance of speech. Scattered retinal hemorrhages were seen about the right disk. During examination the patient vomited several times.

On lumbar puncture grossly bloody spinal fluid under increased pressure was withdrawn, with temporary relief of the headache. The spinal-fluid Wassermann test was positive, the blood Hinton test was positive, and the Wassermann doubtful. A week after admission, the number of red cells in the spinal fluid had decreased and the fluid had become xanthochromic. A week before discharge, the spinal-fluid Wassermann test was negative.

The patient was discharged six weeks after admission.

Second admission (three months later) The patient again complained of headache and was readmitted. The pain occurred daily, usually being present when the patient awoke, continuing for about an hour and then gradually subsiding. It was referred to the occipital region and radiated down both sides of the neck and occasionally to the forehead. During such an attack the neck was sore but not stiff. There had been no visual disturbances.

The fundi were normal. A soft diastolic murmur

was heard over the tricuspid area. The blood pressure was 130 systolic, 78 diastolic. The tendon reflexes were still more active on the right than on the left. The plantar responses were normal.

The blood Hinton reaction was positive, and the Wassermann negative.

He was discharged improved after four weeks.

Third admission (one year later) The patient was readmitted because of fatigue and slight exertional dyspnea of several months' duration and moderately acute dyspnea and orthopnea for one day.

On entry the blood pressure was 142 systolic, 55 diastolic. The heart was enlarged to the left axillary line. A loud, harsh systolic murmur was heard along the left border of the sternum, with a loud, blowing diastolic murmur over the same area. Numerous moist rales were heard at the lung bases. A Corrigan type of pulse and capillary pulsations were noted.

An x-ray examination of the chest showed that the heart was moderately enlarged in the region of the left ventricle, with a transverse diameter of 18.5 cm. and an internal chest diameter of 32.2 cm. The aorta was tortuous and moderately dilated. The lung fields were clear. The diaphragm was smooth and showed a normal excursion.

An electrocardiogram showed regular rhythm at a rate of 55, a PR interval of 0.18 second, sagging ST₁ and ST₂, diphasic T₁, inverted T₂, upright T₃, low T₄, and moderate left-axis deviation. The QRS complexes were slightly blurred, measuring up to 0.10 mm. The blood Hinton and Wassermann reactions were both positive.

He was discharged on the ninth hospital day.

Final admission (one year later) One week before readmission the patient, at that time sixty-six years old, noticed pain high in the epigastrium radiating upward to the base of the neck and anteriorly just above the sternal notch. He perspired profusely, but there was no change in pulse, respirations or blood pressure. This attack lasted about thirty minutes, and the pain was relieved by nitroglycerin. The following night two similar attacks occurred, but they were less severe than the first, these were also relieved by nitroglycerin. Twenty-four hours later a fourth attack occurred, and at that time a physician found epigastric tenderness. The heart beat was less vigorous than previously, but the pulse was slow and regular. The following day he felt well and went to work. Five days later, in the evening, pain again developed in the suprasternal notch, but without accompanying pain in the epigastrium. A short time later numbness appeared in the left foot and gradually spread up the left leg. This numbness was soon followed by excruciating pain in the same distribution. Numbness later appeared in the right foot, but lasted only thirty minutes and was not followed by pain.

On admission the patient was in great pain, perspiring profusely. The heart beat was regular, at a

annulus fibrosus of the valve, completely surrounding the mouths of both coronary arteries. There was also dissection distally throughout the entire aorta down into the iliac arteries. The aneurysm occluded the left femoral artery by the contiguity of the raised intima on one side of the vessel against the opposite side of the vessel. There were also dissections for short distances into some of the major branches of the aorta, such as the renal, splenic and internal carotid arteries.

It seemed to us at the time of autopsy, and our sections confirmed it, that the hemorrhage in the dissecting aneurysm around the valve was older than that in the part of the dissecting channel above the tear. I believe, therefore, that the initial pain that the patient had a week before admission was due to the proximal dissection, which surrounded the mouths of the coronary vessels and gave him real anginal pain, the attacks during the following week being due to the blood clot around the coronary arteries. The final episode occurred when the dissection progressed distally to produce the peripheral occlusion. His death was due to an external rupture through the adventitia into the pericardium and to cardiac tamponade.

DR HARWOOD: Could the aneurysm around the valve explain the disappearance of the diastolic murmur?

DR WHITE: Was it striking?

DR HARWOOD: Yes.

DR CASTLEMAN: I do not know how to explain the murmurs. We found no evidence of syphilitic aortitis. There was no separation of the aortic cusps at the commissures to account for the regurgitation. In fact there was interadherence between adjacent cusps for a distance of 5 mm, such as one sees in rheumatic heart disease. There was no gross intimal scarring, and no microscopic evidence in the media suggestive of syphilitic aortitis. We cut many sections but have not been able to prove that the patient had syphilitic aortitis. Certainly, if he had it, it was minimal.

The heart weighed 700 gm. The base of the posterior papillary muscle in the left chamber was grayish to yellowish white, and microscopically it showed infarction of three or four weeks' duration — long before the first acute attack. In addition, the tip of the papillary muscle showed an infarction that would fit in with a week's duration. I suppose that the coronary circulation to the papillary muscle had been impaired before he had the aortic-wall dissection and that the hemorrhage around the coronary vessels produced anoxia of the heart to produce further damage to the tip of the papillary muscle. The main coronary arteries showed only moderate sclerotic changes.

DR WHITE: Could you tell whether the aorta was dilated just above the aortic valve?

DR CASTLEMAN: It was slightly dilated.

DR WHITE: That might then have been from

some process, such as senile weakness of the wall, other than syphilitic aortitis, with or without separation of the aortic cusps.

DR CASTLEMAN: You mean senile ectasia?

DR WHITE: Yes. What about the cerebral symptoms?

DR CASTLEMAN: We were unable to obtain permission to examine the head.

DR WHITE: Will you answer the question that I raised about the circle of Willis?

DR CASTLEMAN: I do not believe that we have ever seen these symptoms due to syphilis, and I should feel that it was probably on the basis of a congenital aneurysm rather than of a pachymeningitis due to syphilis. Pain in the back of the neck is not at all infrequent.

DR WHITE: The terminal electrocardiogram in this case pointed to the diagnosis of dissecting aortic aneurysm rather than to that of extensive myocardial infarction.

CASE 31392

PRESENTATION OF CASE

First admission. A sixty-year-old woman entered the hospital complaining of pain and swelling in the legs of about ten years' duration. The pain came on when she stood for several hours at a time. Her health had otherwise been good. The blood pressure was 195 systolic, 110 diastolic. The left pupil was larger than the right. The heart and lungs were normal. Bilateral varicosities of the great saphenous system were ligated and injected. The patient recovered uneventfully and was discharged after two days.

Final admission (eleven years later). For five years after discharge the patient was followed in the Out Patient Department, other varices of the legs having been injected from time to time. Six years before readmission she presented a skin eruption of two months' duration. It consisted of red papules and nodules, with serpiginous outlines, 0.5 cm in diameter, which were scattered over an area 5 by 7 cm on the left elbow. Similar lesions were seen on the inner aspect of the thighs, with slight scaling in these locations, and on the right elbow. The Hinton and Wassermann tests were strongly positive. The patient denied venereal disease and gave no history of previous skin lesions. During the next three months the eruption subsided. The patient refused a lumbar puncture and permitted only a limited physical examination. The blood pressure was 150 systolic, 76 diastolic. The pupils were large and slightly irregular but reacted to light and accommodation. The nasal septum was intact. There were no cardiac murmurs. The reflexes were normal. The patient kept no appointments for antisypilitic therapy, and her case was considered to be closed.

heard was less intense than it had been, owing to heart failure "The left lower extremity was white and paralyzed, with no sensation or reflexes" That was the event that precipitated death, evidently an acute obstruction of the circulation of the legs, complete on the left and partial on the right There are two explanations that are more probable than others In the first place it could have been a massive embolus to the bifurcation of the aorta from an intracardiac thrombosis over the site of a myocardial infarct caused either by obstruction of a coronary artery because of an arteriosclerotic process or by occlusion of the ostium of the coronary artery by syphilitic aortitis, or possibly by both conditions Or the answer could be an extensive dissection of the aorta occurring in stages, with or without final rupture Death in either case could be ascribed to ventricular fibrillation rather than to terminal hemorrhage

In summary, I believe that this case illustrates the evolution, rather late in life, of cardiovascular syphilis involving the cerebral circulation and aorta in particular, with the development of aortic regurgitation, left ventricular enlargement, dilatation and failure, and probably coronary ostial occlusion with myocardial infarction from that source rather than from a coincident coronary involvement, the terminal event was probably an embolic occlusion of the aortic bifurcation from intracardiac thrombosis, but possibly it was a progressive dissection of the aortic wall with occlusion of the coronary and left iliac arteries, followed by terminal cardiac tamponade from aortic rupture I favor the former alternative I do not recall having seen any cases of dissecting aneurysm with syphilitic aortitis as a background, but there are exceptions and this may be one of them There remains the possibility of arteriosclerotic occlusion superimposed on syphilitic aortitis

This final electrocardiogram (presented by Dr Harwood), taken a few minutes before the patient died and about a week after the onset of pain, shows many ventricular premature beats in Leads 1 and 2, with bigeminal rhythm in these two leads The rate is 65 or 70, with full-length conduction time (about 0.2 second), it should not be interpreted auriculoventricular block There is slight left-axis deviation, with distinct sagging of the ST segments in Leads 1 and 2 and in Leads CF₁ and CF₂ The T waves are low throughout, especially in the limb, but they are upright in all three precordial leads (Leads CF₃, CF₄ and CF₆) There is still the probability that digitalis rather than acute myocardial infarction was responsible for at least a certain amount of the sagging of the ST segments There is no marked elevation of the ST segments in any leads Was he still getting digitalis?

DR HARWOOD Yes

DR WHITE Whether the bigeminal rhythm can be ascribed to the digitalis is open to question

There was no indication clinically that he was toxic from digitalis?

DR HARWOOD No

DR WHITE This final electrocardiogram clearly supports the diagnosis of a dissecting aortic aneurysm rather than that of myocardial infarction with embolic blocking at the aortic bifurcation, but I am not sure that it rules out the latter condition completely

DR HARWOOD This case presented a problem of immediate therapy The patient did not appear particularly ill He had the most excruciating pain during the last two hours of his life I had not been able to make up my mind what the matter was The pain was above the sternal notch and passed deep into the sternum It resulted in profuse perspiration As soon as the pain disappeared the patient felt perfectly well When the pain and ischemia of the left leg appeared, along with pain in the throat, I again thought, as I had once or twice during the previous week, of the possibility of dissecting aneurysm On the other hand he had obtained some relief from nitroglycerin, and the possibility of myocardial infarction, perhaps from syphilitic involvement of the coronary arteries, could not be excluded I talked with a surgeon who had had considerable experience with vascular occlusion of the lower extremities, and he agreed that we ought to get the patient into the hospital and make an attempt to remove the embolus if one was there The patient did not survive long enough for the surgeon to see him

CLINICAL DIAGNOSES

Coronary thrombosis, with myocardial infarction
Embolism to bifurcation of aorta -
Syphilitic aortitis

DR. WHITE'S DIAGNOSES

Coronary occlusion due to syphilitic obstruction of mouths of coronary arteries
Occlusion of left iliac artery due to embolus at bifurcation of aorta from intracardiac thrombosis or to dissecting aortic aneurysm with terminal rupture and cardiac tamponade

ANATOMICAL DIAGNOSES

Dissecting aortic aneurysm, with involvement of coronary mouths, occlusion of left femoral artery and rupture into pericardium
Hemopericardium and cardiac tamponade
Cardiac infarction, left papillary muscle
Cardiac hypertrophy
Endocarditis, chronic rheumatic aortic valve

PATHOLOGICAL DISCUSSION

DR CASTLEMAN The autopsy showed a dissecting aortic aneurysm The intimal tear occurred in the usual place, about 2 cm above the aortic valve, and there was dissection proximally down to the

line. In the x-ray report nothing is said about the size. I should like to look at the films

DR. MILFORD D. SCHULZ The heart does not appear to be enlarged. I wonder about all these prominent lung markings. They are probably best explained by pulmonary edema, but lymphatic spread of metastatic carcinoma cannot be ruled out.

DR. KLEMPERER So the evidence is against a failing syphilitic heart, and there must have been some other cause for her death. Could cardiac failure alone explain the terminal episode? Was cardiac failure present at all? I believe that cardiac failure was proved by the nature of the respirations, by the rales in the chest and by the large liver. I should like to know whether the neck veins were distended. I assume that they probably were, although nothing is said about them. Cardiac failure alone would not explain the rapid and marked rise in the nonprotein nitrogen. The nonprotein nitrogen may go up slightly in congestive failure, but not to that extent. The rest of the blood chemical findings could also be explained only on the basis of renal embarrassment. There was definite chloride retention, with corresponding reduction in the carbon dioxide content. The low total protein, with reduction in albumin, is consistent with renal disease and was a contributing cause of this patient's edema. The calcium was low, but this figure could have been accounted for by reduction in serum protein. I conclude that the patient had renal disease, as well as cardiac failure that was not fully accounted for by aortic regurgitation.

This patient was seventy-one years of age and was known to have had a blood pressure of 195 systolic, 110 diastolic, eleven years before admission, which means a long-standing hypertension, although a lower reading was obtained at one time. She would be likely to have had hypertensive and arteriosclerotic heart disease. It might be that this patient who had syphilitic involvement of the aorta also had involvement of the orifices of the coronary arteries. We might also consider the rare case of syphilitic involvement of the coronary arteries themselves. There is no evidence to make such a diagnosis, and in the absence of an electrocardiogram, I am inclined to explain the cardiac failure by the combination of aortic regurgitation and hypertensive and arteriosclerotic heart disease.

It remains to discuss the nature of the renal lesion. At the onset of the first symptoms of renal failure the patient was receiving bismuth. Bismuth is a heavy metal and, like mercury, is able to produce renal lesions that consist in degeneration and necrosis of the tubular epithelium. This condition is extremely rare in human beings and is known mostly from experimental studies in animals. Doses that are toxic in animals are many times the therapeutic doses. We do not know exactly how much bismuth she had been getting. I must assume that the 1 gm. given every two weeks refers to the com-

pound and not to the metal, thus representing the conventional therapeutic dose of bismuth. This, however, remains uncertain because we know nothing about the solubility of the drug given. By and large not more than 200 mg. of metal are given weekly if the compound is insoluble. In the absence of direct information I must assume that the treatment was proper and, as such, not the cause of fatal nephritis. In addition, patients who have bismuth nephritis usually develop other toxic symptoms, such as a bismuth line and severe stomatitis. Renal failure as the only sign of bismuth poisoning is not known to me.

There are two kinds of renal disease thought to be due to syphilis. One, the nephrotic syndrome, usually appears early in the disease and rapidly improves on treatment. The other is the interstitial involvement of the kidneys described by Rich¹ in 1932. Little is known about the clinical signs and symptoms of the latter syndrome, and only a few cases have been described in which uremia was due to this kind of renal involvement. I believe that there is a definite possibility that the patient had this kind of interstitial nephritis, which is thought to be due to syphilis, but it seems more probable that she suffered from renal disease coincident with syphilis. She could possibly have had vascular nephritis, — she was known to have had long-standing hypertension, — but I doubt this, because at first she was able to concentrate urine well. That should not be possible in vascular nephritis of long standing. The patient's disease was rapidly progressive, whereas vascular renal lesions are usually slow in their development.

Did she have glomerulonephritis? Again, we cannot rule it out, but there is no history of acute disease preceding the chronic stage. It may have been subacute, but if the lesion is sudden and progressive, as this one was, I should expect anemia, which this woman did not have. The likeliest cause for the renal failure seems to have been a pyelonephritis. She was known to have had a colon-bacillus infection. She had costovertebral angle tenderness. The clinical course was consistent with this concept, and the urinary findings were also in keeping. I therefore believe that pyelonephritis was the cause of renal failure, although I cannot rule out syphilitic nephritis.

A few things remain to be answered. Did this patient have cerebrospinal syphilis? We have only a few points to go by, and a spinal-fluid examination was not performed. Eleven years before admission the left pupil was larger than the right. In the absence of any other neurologic signs I should not pay too much attention to it, although transient neurologic signs about the eyes are not infrequent in early central-nervous-system syphilis. If this had been due to syphilis I should have expected more rapid progression of the central-nervous-system disease. Later we hear about ptosis, and if this was

Five years later, at the age of seventy-one, she returned to the hospital complaining of swelling of the legs. One and a half years before readmission an eruption appeared on the left forearm. Elsewhere she had been given potassium iodide and 1 gm of intramuscular bismuth every two weeks for the four months before admission. A urinalysis done before her seventh bismuth injection showed no abnormalities, but shortly after it she noticed swelling of the legs and abdomen and pain in the back. She was somewhat nauseated but did not vomit. During the development of the swelling she gained 20 pounds in weight. She had had exertional dyspnea for about six months.

Physical examination revealed a fairly well developed and nourished woman, with rapid shallow respirations. There was marked pitting edema of the lower extremities extending up the back and the abdominal wall to the level of the xiphoid. The skin showed senile keratoses and areas of increased pigmentation on the legs. A diffuse, hazy scarring was seen in the center of the cornea of the left eye, and there were some fibrous strands over the lens of the right eye. The pupils reacted to light. The eye movements were normal, but right ptosis was present. The eyegrounds were normal. The superficial lymph nodes were not enlarged. There was tenderness to percussion over the left chest. The breasts were normal. Rales were heard throughout both lung fields. Resonance and breath sounds were decreased over both bases. The apex of the heart was percussed 9.5 cm to the left of the midline. A blowing diastolic murmur was heard along the left sternal border. Rumbling presystolic and systolic murmurs were heard at the apex. The liver was palpable two fingerbreadths below the right costal margin. The spleen was not palpable. The abdomen was distended, and shifting dullness was elicited. Neurologic examination was negative.

The temperature was 97°F, the pulse 70, and the respirations 20. The blood pressure was 180 systolic, 90 diastolic.

Examination of the blood revealed a red-cell count of 4,000,000, with 13.5 gm of hemoglobin, and a white-cell count of 5900, with 72 per cent neutrophils. The nonprotein nitrogen was 50 mg per 100 cc, the fasting blood sugar 99 mg, and the protein 4.6 gm, with 2.0 gm of albumin and 2.6 gm of globulin. The carbon dioxide was 21.8 milliequiv per liter, and the chloride 108 milliequiv. The urine had a specific gravity of 1.022 and gave a +++ test for albumin, the sediment contained 5 red cells, 10 white cells and many hyaline casts per high-power field. Urine culture showed numerous colonies of colon bacillus. The nonprotein nitrogen rose steadily to 136 mg per 100 cc, and the carbon dioxide fell to 14.6 milliequiv per liter. The serum calcium was 7.7 mg per 100 cc, and the phosphorus 5.7 mg. The serum sodium was 125.2 milliequiv per liter, and the potassium 4.5 milliequiv. A cephalin

flocculation test was ++ in twenty-four hours and +++ in forty-eight hours. A blood Hinton test was positive.

An x-ray film of the chest showed an abnormally high diaphragm, with a question of fluid in the abdomen. The heart was transverse in position. There was considerable increase in the lung markings. The pleural sinuses were obliterated. A lateral view showed no definite areas of consolidation.

The patient continued to complain of nausea. On the tenth hospital day the temperature rose to 102°F and the white-cell count to 13,000, with 98 per cent neutrophils. Tenderness was elicited in the costo-vertebral angles and in both calves, being more marked on the right than on the left. Crackling rales were heard over the lungs, but there was no evidence of pleural effusion. Several plasma transfusions were given. An abdominal paracentesis was done, and 2800 cc of turbid yellow fluid was withdrawn, the sediment showed no tumor cells.

On the eighteenth hospital day the cardiac murmurs became much louder than previously, with a questionable pericardial friction rub. The skin was cold and moist, and the blood pressure 88 systolic, 44 diastolic. The patient became irrational but also complained of epigastric pain and vomiting. As a plasma transfusion was being given she gasped and expired.

DIFFERENTIAL DIAGNOSIS

DR. FRIEDRICH W. KLEMPERER. One thing seems to be certain about this patient, namely, she had syphilis. She came to the hospital because of a skin rash, which raised the suspicion of syphilis, and since that time she had been known to have persistently positive Wassermann and Hinton reactions. I do not believe that, in the presence of these persistent reactions, there can be any doubt about this patient's having syphilis. She developed an aortic diastolic murmur. In the presence of syphilis the most reasonable diagnosis would be syphilitic aortic regurgitation, but a presystolic and systolic mitral murmur were also heard. One might think of rheumatic heart disease involving the mitral and aortic valve. The heart disease, however, developed late in life, and we know that on previous occasions she had not had murmurs. Rheumatic heart disease does not develop as a rule at this time of life. The mitral murmur must be explained as an Austin Flint murmur, which is a mitral diastolic murmur heard in aortic regurgitation. It was probably due to dilatation of the left ventricle causing a relative stenosis of the mitral ring. Granted she had syphilitic aortic regurgitation, could the final illness be explained on the basis of failure due to this disease? If the heart failed because of syphilitic aortic regurgitation one would expect it to be extremely large. Physical examination does not bear that out, the heart was percussed 9.5 cm to the left of the mid-

DR CASTLEMAN They were heard by many examiners

DR. WHITE The murmurs were heard at entry How long was the patient in the hospital?

DR. CASTLEMAN Almost three weeks

DR. WHITE It is certainly possible to have a to-and-fro pericardial friction rub that resembles murmurs, but it rarely lasts over so long a period of time.

DR. CASTLEMAN. A note was made on the sixteenth day that the heart murmurs were much louder than they had been, with a question of pericardial rub

DR. WHITE Do you think she had the pericardial involvement throughout her hospital stay?

DR. CASTLEMAN No

believes that a presystolic murmur can be explained on the basis of an Austin Flint murmur

DR. WHITE Dr E P Bagg, of Holyoke, raises the question whether temporary dilatation of the heart could have been responsible for the murmurs at first. Evidently the staff did not find much dilatation of the heart clinically We cannot settle that question The x-ray film did not show much of any enlargement

I agree that the Austin Flint murmurs that I have heard have, as a rule, been in patients who have had marked enlargement of the heart with free aortic regurgitation, due either to syphilis or to rheumatic involvement In cases with rheumatic involvement one wonders, of course, if there is not some actual mitral stenosis in addition My con-



FIGURE 1 Photomicrograph of Kidney Showing Tubular Degeneration and Intranuclear Bodies

DR. WHITE There remains then some question concerning the exact cause of the murmurs

DR. T. DUCKETT JONES I should like to ask Dr White about the Austin Flint murmur

This patient never had any evidence of free aortic disease, and one does not hear an Austin Flint murmur unless there is an extremely large heart practically always with free aortic disease and definite evidence of regurgitation I wonder if Dr White would be willing to describe the Austin Flint murmur I have read the original description² over and over, and I have tried to apply it in a number of cases Often it is in a case in which there is a presystolic murmur, which is, so far as I know, characteristic of mitral stenosis, but I cannot conceive of an aortic process that causes a presystolic crescendo because of the mechanism that it requires Mitral disease can also produce rumbles in diastole I wonder if that is Dr White's idea or whether he

ception of the murmur is that it is due, not as originally explained to the pressure of the regurgitant stream of blood going through the aortic valve and compressing the anterior cusp of the mitral valve, thereby producing a functional stenosis, but rather, as Dr Klemperer has said, to the relative stenosis of the normal mitral ring in comparison with the size of the dilated ventricular cavity This state of affairs can exist in the cases just cited and in other patients with left ventricular dilatation without aortic regurgitation, in either case there would be the same murmur Years ago, Dr Jones, Dr Bland and I⁴ described, in certain cases of acute or subacute rheumatic myocarditis, mitral diastolic murmurs due to such relative mitral stenosis without aortic regurgitation, but in those cases the heart was big and the murmur disappeared when the heart became smaller

The best Austin Flint murmurs that I have heard

definite, it should be explained. In this case it may easily be explained on the basis of central-nervous-system syphilis, which I think the woman had. The question of cancer was apparently raised by the physician who had the sediment from the ascitic fluid examined in the laboratory. The fluid was described as turbid. If she had an extremely turbid fluid I should be inclined to think that she had destruction of the lymphatic vessels due to malignancy, slightly turbid fluid is not significant. We do not know anything about the specific gravity. I do not see any reason to introduce a new factor in this already complicated picture.

DR JACOB LERMAN: Would you like to explain the low serum sodium? I am confused by the values.

DR KLEMPERER: I was somewhat confused myself, because the sodium should fairly well balance the chloride and carbon dioxide. It does not, but I cannot explain this.

DR LERMAN: Why did they give transfusions?

DR KLEMPERER: I do not understand that either. On the basis of the data given in the record, one would think that this woman had failure of the left ventricle. If plasma transfusions are given, the patient's blood volume is increased, not only by the amount of fluid given but also by the amount of water drawn into the circulation by the increased osmotic pressure produced by the plasma. The total increase in blood volume may easily overtax an already failing left ventricle. As a matter of fact, this woman died suddenly during a transfusion and, I believe, in pulmonary edema, which may have been related to the transfusions.

CLINICAL DIAGNOSES

Syphilitic nephritis

Syphilitic aortic regurgitation

DR KLEMPERER'S DIAGNOSES

Syphilitic aortic regurgitation

Hypertensive and arteriosclerotic heart disease

Pyelonephritis?

Syphilitic nephritis?

Syphilis of the central nervous system

ANATOMICAL DIAGNOSES

Nephrosis, probably due to bismuth intoxication

Syphilitic aortitis

Septicemia (Type 17 pneumococcus)

Pericarditis, fibrinous

Pulmonary edema and congestion

Portal cirrhosis

Ascites

Esophageal varices

PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMAN: The autopsy on this patient showed about 2500 cc of ascitic fluid, which was probably due to an advanced portal cirrhosis.

The liver weighed only 900 gm and was extremely nodular. She had probably had the condition for years. The spleen was somewhat enlarged, and in the esophagus we found numerous varices, although there was no evidence of hemorrhage from them. The heart was small, weighing only 220 gm, with perhaps slight hypertrophy of the left side. All the valves looked reasonably good. We found no evidence of separation of the aortic cusps at their commissures and no evidence of insufficiency. There were, however, a number of the congenital perforations of the cusps that we see so often. I feel sure that they had nothing to do with the murmurs that were heard. Syphilitic aortitis was present throughout the aorta but not around the mouths of the coronary arteries or in the region of the cusps themselves, and consequently there was no scarring.

DR PAUL D WHITE: Do you not believe that there was enough aortitis to dilate the aorta above the valve and in that way to be responsible for the murmur during life?

DR CASTLEMAN: Possibly, that is the only explanation for the murmur.

DR WHITE: Evidently there was no marked aortic dilatation post mortem.

DR CASTLEMAN: No. The lungs showed acute congestion and edema. The kidneys were not remarkable grossly. They weighed about 120 gm each, somewhat smaller than normal, and they showed slight scarring due to vascular disease. Microscopically, however, we found evidence of severe tubular disease. The convoluted tubules showed marked degeneration, granularity and necrosis of the epithelial cells (Fig 1). Another finding in the tubules was the presence within some of the nuclei of globular refractile bodies. These bodies were described years ago by Pappenheimer,² who believed that they were the result of bismuth intoxication. He later produced the disease experimentally in rats by injecting a bismuth solution. I am certain that these are the same refractile bodies that Pappenheimer found in his cases. We looked carefully for the type of syphilitic kidney disease that was described by Rich but were unable to find any evidence of it. On the other hand, I suppose that one cannot rule out the other type of syphilitic disease of the kidney, the so-called "syphilitic nephrosis," but I am inclined to believe that the lesions are better explained on the basis of bismuth intoxication, that is, a toxic nephrosis of the tubular epithelium due to the bismuth injections. There was no evidence of pyelonephritis or glomerulonephritis. There were a few vascular scars, but no significant nephrosclerosis. She did have a septicemia, which was due to a Type 17 pneumococcus. There was also a fibrinous pericarditis. Could the murmurs in some way have been accounted for by the pericarditis?

DR WHITE: Who heard the murmurs, and were they confirmed by the visiting staff?

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UNITED WAR FUND

WHEN a patient passes the crisis of a serious illness, the physician does not cross the case off his list but maintains a watchful vigilance to aid convalescence and to guard against relapse. In the same way, a nation cannot completely abandon, at the close of a war, certain services, both home and abroad, since these activities must continue through the long period of reconversion.

The Victory Campaign of the Greater Boston United War Fund, which will be conducted October 1 to 17, has a goal of \$7,750,000 to help maintain such services. By supporting the coming campaign, physicians in Greater Boston can show that they are not deserting the agencies that administer

to the wounds opened by war—they can show they are not ignoring the appeals of the USO, the United Seaman's Service and the groups that give relief to peoples in war-devastated lands. Most important of all, support of the Fund means that they appreciate the value of its Red Feather community services, which must be ready to serve any of the quarter million returning servicemen and servicewomen who need them. It means that they will not fail the social and health centers and the youth and old-age services, which are so necessary to combat the aftershock of war and to keep the Nation healthy.

By endorsing the Fund, the physicians of Greater Boston will once more give whole-hearted support to their communities and to the world beyond.

RELEASE OF MEDICAL OFFICERS

FOR a considerable number of combat troops who have seen long service in Europe or in the Pacific some provisions have already been made for orderly release to a civilian status. No official information is available, however, to indicate how soon the majority of medical officers and nurses may expect demobilization. The provisions for the release of men over forty do not apply to officers, particularly those in the Medical Corps. Surgeon General Kirk, in a press and radio conference late last May, let out more than a hint concerning the immediate outlook in this respect. In the course of a review of the excellent state of the health of the Army in this war as compared with that in previous ones, he made the following pertinent statements:

The Medical Department today is well prepared for the intensification of its work brought about by the cessation of hostilities in Europe. Thousands of wounded veterans in the European and Mediterranean theaters are being transported to the United States as fast as ships and planes are available.

The peak of the Medical Department's activities will not be reached until the fall of 1945. At present, wounded and sick are being returned to this country from all theaters at the rate of 44,000 a month. This evacuation will continue until all of the patients in the European and Mediterranean theaters are removed, which will require ninety days.

The arrival of these thousands of wounded and sick in this country during the next three months will place a heavy load on our general and convalescent hospitals.

were in Atlanta when I was attending a clinic of cases of well marked, free aortic regurgitation in syphilitic aortitis. Here in New England relatively few Austin Flint murmurs are heard.

I think that I have noted only infrequently a presystolic accentuation at the end of the mid-diastolic murmur of the Austin Flint type. The auricle in contracting can increase the speed of the blood flow through the mitral ring just before ventricular systole and so theoretically, as well as apparently actually, can increase the murmur started by the simple flow of blood through the valve from auricle to ventricle earlier in diastole, but this presystolic accentuation is not so frequent as accentua-

tion of the middiastolic part of the murmur. Of course in most cases with mitral stenosis *per se* and in all such cases with auricular fibrillation, the murmur is mid-diastolic only. In cases with marked presystolic accentuation, the murmur is generally not an Austin Flint murmur.

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CITY OR TOWN	HOSPITAL	RESPIRATORS
Beverly	Beverly Hospital	2
Boston	Boston City Hospital	8
	Children's Hospital	Several
	Forest Hills General Hospital	0
	Haynes Memorial Hospital	3
	Massachusetts General Hospital	4
	New England Hospital for Women and Children	0
	(will only accept emergency cases)	
	Peter Bent Brigham Hospital	3
	(will accept patients over 12 years of age and those younger only in an emergency)	
Brookline	Brooks Hospital	0
Cambridge	Cambridge City Hospital	1
	(will only accept emergency cases)	
Fall River	Fall River General Hospital	1
	Union Hospital	1
Fitchburg	Burbank Hospital	1
	(will only accept local cases)	
Greenfield	Greenfield Isolation Hospital	1
Haverhill	Haverhill Municipal Hospital (Hale)	1
	(will accept a limited number of local cases)	
Holyoke	Holyoke Hospital	1
Lawrence	Lawrence General Hospital	2
Leominster	Leominster Hospital	2
Lowell	Shaw Hospital	0
	St. John's Hospital	2
Malden	Malden Hospital	1
	(local cases preferred)	
Nantucket	Nantucket Cottage Hospital	0
New Bedford	St. Luke's Hospital	1
Newburyport	Anna Jaques Hospital	0*
Newton	Newton-Wellesley Hospital	1
Pittsfield	House of Mercy Hospital	1
Pocasset	Barnstable County Sanatorium	0
Quincy	Quincy City Hospital	2†
Salem	Children's Hospital	2
Springfield	Health Department Hospital	1
	Mercy Hospital	0
	Springfield Hospital	0
Worcester	Belmont Hospital	1
	Memorial Hospital	1
	Worcester City Hospital	3

*Newburyport Board of Health has applied for a respirator

†One adult and one infant respirator

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Salem	October 1	Paul W. Hugenberger
Haverhill	October 3	William T. Green
Lowell	October 5	Albert H. Brewster
Brockton	October 11	George W. Van Gorder
Pittsfield	October 15	Frank A. Slowick
Springfield	October 16	Garry deN. Hough, Jr.
Worcester	October 19	John W. O'Meara
Fall River	October 22	Eugene A. McCarthy
Hyannis	October 23	Paul L. Norton

NOTES

Caroline A. Chandler, M.D., has been appointed supervisor of Clinics for Crippled Children, Services for Crippled Children, Massachusetts Department of Public Health. Prior to accepting a commission in United States Public Health Service, Dr. Chandler was with the Division of Research in Child Development, Children's Bureau. She is certified

by the American Board of Pediatrics and is a member of the Academy of Pediatrics.

Roy F. Feemster, M.D., has been appointed director of the Division of Local Health Administration, Massachusetts Department of Public Health. He will retain this office for the duration of the military emergency, after which he will return to his former position of director of the Division of Communicable Disease.

Merrill E. Champion, M.D., former epidemiologist in the Massachusetts Department of Public Health, is now acting director of the Division of Communicable Disease.

A Laurence Corbman, D.D.S., formerly associate dental surgeon with the Office of Indian Affairs, United States Department of the Interior, in South Dakota, has been appointed public-health dental supervisor with the Massachusetts Department of Public Health. He is assisting in a dental-caries study recently authorized by the Legislature in which the use of fluorine for reducing caries among school children is being investigated.

MISCELLANY

TUBERCLE BACILLI IN GASTRIC CONTENTS

Any evidence that helps to answer the question of whether or not a patient under treatment for tuberculosis is a source of danger to others is of vital value to the physician, the patient and the public. The examination of gastric contents for the presence of tubercle bacilli is rapidly becoming an essential procedure in those cases in which other tests fail to give a clear-cut answer (Feld, D. D. Significance of tubercle bacilli in gastric contents. *Am. Rev. Tuberc.* 50: 481-489, 1944).

Examination of gastric contents for tubercle bacilli in the fasting patient, although a routine procedure among children at Muirdale Sanatorium since its inception, has only gradually been extended to adults. The now demonstrated importance of the procedure in aiding diagnosis, in guiding therapy, and in evaluating the patient before discharge has come to be recognized rather slowly.

Examination of gastric contents for tubercle bacilli is used by the author on all patients who deny raising sputum or whose sputum is negative. It is also used in cases in which there is doubt concerning the source of the sample presented. Since a single negative gastric aspiration is not considered conclusive, repeated aspirations are performed at intervals. Some patients have cultures of both sputum and gastric contents. Such a procedure expedites the diagnosis of cases with suspected active lesions.

The material used for examination consists of undiluted gastric contents aspirated from fasting patients the first thing in the morning. Previous to 1941, culture and guinea-pig inoculation were done simultaneously on all specimens. Since then only cultures have been used, because they are very accurate and the difference in the results of the two procedures did not warrant continued use of the guinea pig. All specimens are cultured on three slants of Petragnani's medium, and contamination is reported when all three tubes are involved, an infrequent occurrence.

One cannot rely on smears of concentrated specimens of gastric contents for the detection of tubercle bacilli—the number of positives is always small. In certain diagnostic cases animal inoculations, in addition to cultures, are necessary.

The patient who has negative sputum cultures but who has tubercle bacilli only by gastric examination, is not a so-called "innocuous patient." In our survey we observed 21 such patients who on subsequent sputum examination were positive on concentrated smear or culture. Therefore, these patients can and do develop subsequent positive sputum

The population of all Army hospitals in the United States at present is 290,000. By September, this is expected to reach 315,000, taking into consideration the discharge rate.

It can readily be seen that the Medical Department will be operating at capacity for many months to come, and there will be a critical need for its professional and civilian personnel during this period.

From these remarks it may be inferred that few medical officers and nurses can anticipate early release from service as a result of the victorious conclusion of the war. Doubtless some men who have been taken from key positions in hospitals and medical schools will be relinquished within a reasonable time if sufficient and pressing need for their services is shown, and the office of the surgeon-general has recently indicated that medical officers returned by a theater or declared surplus by a major force, provided their Adjusted Service Ratings are sufficiently high or provided they are over 50 years of age, are eligible for discharge. The majority will have to wait for an undetermined period.

Perhaps the most discouraging news for the medical personnel, although it is proportionately more heartening to the rest of the men in the service, is contained in General Kirk's closing remarks:

Illness and recuperation of wounded and injured men does not cease with a formal declaration of the end of hostilities on any front. The care of those men and women is a continuing responsibility of the Medical Department, which will go on for many months in the future. It will increase rather than diminish.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON LEGISLATION

Reprints of articles appearing in the June 2 issue of the *Journal of the American Medical Association*, relative to the Wagner-Murray-Dingell Bill, have recently been sent to each member of the Society.

Constructive comments as to how the Committee on Legislation can best handle this situation will be greatly appreciated by the committee.

HUMPHREY L. MCCARTHY, *Chairman*

DEATHS

BRODRICK — Francis S. Brodrick, M.D., of Boston, died September 11. He was in his seventy-eighth year.

Dr. Brodrick received his degree from Wayne University College of Medicine, Detroit, in 1895. He was assistant superintendent of the Boston City Hospital for twenty-five years, having retired in 1937.

GRISWOLD — Merton L. Griswold, M.D., of Uxbridge, died June 10. He was in his seventy-seventh year.

Dr. Griswold received his degree from the University of Vermont College of Medicine in 1896.

His widow and two sons survive.

HARKINS — William J. Harkins, M.D., of Quincy, died August 25. He was in his sixtieth year.

Dr. Harkins received his degree from the University of Vermont College of Medicine in 1911. He was associate laryngologist at the Massachusetts General Hospital and assistant surgeon at the Massachusetts Eye and Ear Infirmary. He was consulting surgeon at the Quincy City, Weymouth, Norfolk County, Milton and Hingham hospitals. He was formerly an assistant professor at Harvard Medical School.

His widow and a son survive.

PALMER — Sarah E. Palmer, M.D., of Boston, died August 23.

Dr. Palmer received her degree from the Woman's Medical College of Pennsylvania in 1880 and was the first woman to be admitted to the graduate course in bacteriology at Harvard Medical School. One of the first surgeons to perform cesarean operations, she inaugurated the surgical service at the New England Hospital for Women and Children in 1900. She was a fellow of the American College of Surgeons.

WORTHEN — Clarence F. Worthen, M.D., of Boston, died August 22. He was in his sixty-sixth year.

Dr. Worthen received his degree from Harvard Medical School in 1908. He was ophthalmic surgeon at the Massachusetts Eye and Ear Infirmary, Boston, oculist at the House of Mercy Hospital, Pittsfield, and ophthalmologist at the Newton Hospital. He was a member of the New England Ophthalmological Society and the Newton Medical Society.

His widow and two brothers survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CARE OF CASES OF POLIOMYELITIS IN GENERAL HOSPITALS

It is generally agreed that cases of poliomyelitis can be cared for by general hospitals because the danger to other patients of spread from an active case is relatively small, certainly much less than that of a case of bacillary dysentery. Since this is so, general hospitals can make a contribution to the care of such patients by agreeing to accept them for hospitalization.

In order to care for such patients, a hospital should have on its staff a physician well trained in internal medicine or pediatrics, who can direct the diagnosis and treatment of the disease. The hospital should also have a respirator and at least one person trained in the Kenny technic.

Since it is important that physicians be informed regarding the facilities for the care of poliomyelitis cases, and since the season for an increase in the disease is at hand, the department recently requested information concerning the facilities available throughout the Commonwealth. On the basis of the replies received, the following list of general hospitals that will accept cases of poliomyelitis cases is appended.

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ACUTE PERICARDITIS*

A Graphic Correlation of the X-Ray, Clinical and Electrocardiographic Findings

CAPTAIN DAN L. URSCHEL, M C, A U S, LIEUTENANT PHILIP K. BONDY, M C, A U S,
AND LIEUTENANT COLONEL S. M. SALLEY, M C, A U S

WITHIN a period of three months, 8 cases of pericarditis were treated on the Cardiology Section of the Medical Service at the Battey General Hospital. In studying these patients, a graphic method was devised to correlate the clinical, x-ray and electrocardiographic changes. It was found that the observed alterations followed a variable sequence in different cases—variations that are incompletely described in the textbooks. Inasmuch as the diagnosis of acute pericarditis is often difficult, it is important to discuss thoroughly the variations that may be encountered. It was also noted that patients with purulent pericardial infections, when treated with penicillin and the sulfonamides, followed a different clinical course from that usually described. These cases are therefore presented to emphasize the variable sequence of x-ray, clinical and electrocardiographic findings, and also to demonstrate the relatively benign nature of certain cases of pericarditis when treated by modern methods.

THEORETICAL CONSIDERATIONS

In 1929, Scott, Feil and Katz¹ first described the RS-T elevation occurring early in a case of hemopericardium and in one of purulent pericarditis. At the same time, they² reported the experimental production of changes in the RS-T segment in dogs by the injection of oil or saline solutions into the pericardial sac. They attributed these changes to generalized ischemia of the myocardium produced by pressure. In 1932, Foulger and Foulger³ showed that the electrocardiographic changes produced in such an experiment were temporary unless the intrapericardial pressure was maintained. They demonstrated that the pericardial sac soon stretched, allowing the pressure to fall and the electrocardiogram to return to normal. It was their impression that the change in the RS-T segment was an indication of recent effusion, or of effusion so gross as to prevent further stretching of the pericardial sac. In 1933, Fowler, Rathe and Smith⁴ showed that the T-wave changes in experimental pericarditis

could be correlated with the inflammatory reaction in the subepicardial myocardium. They also showed that when the subepicardial myocarditis had subsided and the inflamed area had been replaced by fibrous tissue, the T waves returned to normal. In 1934, Herrmann and Schwab,⁵ on the basis of experimental work, observed that the early changes in the RS-T segment were due to ischemia of the myocardium, whereas the later T-wave alterations were caused by subepicardial myocarditis. In 1937, Vander Veer and Norris⁶ reported autopsy findings in 10 cases of acute pericarditis. Six of these cases had shown characteristic electrocardiographic changes during the disease, and in all 6 there was definite post-mortem evidence of subepicardial myocarditis. In the 4 cases without characteristic electrocardiograms, 3 showed no involvement of the subepicardial area and 1 had minimal involvement. In 1938, Bellet and McMillan⁷ made histologic studies in 19 cases of acute pericarditis. They also concluded that subepicardial myocarditis was the cause of the electrocardiographic changes. They demonstrated that elevation of the RS-T segment was an extremely transient affair and was especially likely to occur in association with rapidly developing types of pericarditis. In tuberculous pericarditis they found it to be infrequent and usually minor. One of their observations is of particular interest: "Inversion of the T wave was probably associated with the subacute or subchronic stage and occurred when the pericardial process was healing and the general toxemia was less marked." In 1939, Vander Veer and Norris⁸ again discussed the electrocardiographic changes in acute pericarditis and this time included the changes seen in Lead 4R, the chest lead. They reported that the RS-T elevations were very transient, and observed that the electrocardiograms might return almost to normal even though the infection and inflammation of the pericardial sac were continuing and the pericardial effusion was increasing.

In 1940, Noth and Barnes⁹ reviewed the literature up to that time and presented their findings in 53 cases, 25 of which came to autopsy. They ques-

*From the Cardiology Section of the Medical Service, Battey General Hospital, Rome, Georgia.

A patient with a positive gastric content should be treated exactly like a patient with a positive sputum

Before the author's patients are discharged it is necessary that they have negative gastric aspirations in the absence of sputum. This is done to avoid the discharge of active cases. In order for a patient to be discharged with medical advice as inactive he must have at least five successive negative examinations. If negative on those examinations, and if other findings warrant it, the patient is discharged as having no evidence of active disease.

During the past five years, 868 adults at Muirdale Sanatorium had a total of 4204 examinations of gastric contents. Of these, 404 (46.4 per cent) had negative gastric contents, they received 1338 examinations. The remaining 464 (53.6 per cent) cases had 2866 examinations, of which 1271 (44.3 per cent) were positive. The number of examinations per case varied, the average for the negative group being 3.3 per case, and for the positive group 6.2. The number of repeats depends on the individual case, just as in sputum examinations.

Thus there are two groups of patients — those with positive and those with negative gastric contents. Each of these groups in turn is divided into three subgroups: the no-sputum group, the negative-sputum group and the positive-sputum group.

No fine line of distinction can be drawn between these three subgroups. Occasionally patients deny raising sputum and yet the specimens they send in contain tubercle bacilli. Also, there are patients who state they raise sputum, when the sample is only saliva or secretions from a chronic nasopharyngitis common in the locality. It is realized that, if numerous and timely sputum examinations were done, a small percentage would have proved positive. This is not deemed economically advisable, as valuable time may be lost. Instead, a simple reliable gastric aspiration can be done with culture results known in a few weeks.

Significantly, 21 (7.5 per cent) of 282 patients became sputum-positive after being positive at first only on gastric aspiration. This occurred on the average of about six months later. This small group of patients reveals an important fact because, as has been previously pointed out, these cases cannot be considered as harmless, and careful observation and timely sputum examinations will prove that some of these cases are sputum-positive.

It is important to do consecutive gastric examinations on adult patients in whom it is impossible to determine the status of activity from a roentgenogram and in whom the sputum, if present, is negative. If 5 consecutive aspirations are negative on culture, it is likely that there is no evidence of active pulmonary tuberculosis.

Of the 404 patients in our series who never had a positive gastric aspiration, there were 224 who had either no sputum or negative sputum. In spite of the diagnosis of pulmonary tuberculosis on admission the author feels justified in recording a case as having no evidence of active tuberculosis if a series of gastric aspirations is negative, as well as sputum cultures.

The remaining 180 of the 404 with negative gastric contents had, at some time, tubercle bacilli in the sputum. The main reason that there were no positive aspirations in this group is because, in most of these patients, the examinations followed by some ten months a positive sputum, and many of these patients were on the road to recovery.

It is possible, however, to have a negative gastric content and a positive sputum, which does not invalidate the reliability of this procedure. There were several patients who became gastric-content-negative and sputum-negative and then later became sputum-positive. Unstable cases of tuberculosis are likely to fluctuate like this.

In the past year and a half it has been the author's policy to do 5 consecutive aspirations or negative cases. If these examinations are negative by culture, the patient is considered as having no evidence of active pulmonary tuberculosis. In the majority of cases it is wise to hold these patients for observation until the cultures are completed. Of the cultures, over 95 per cent, where positive, will show growth within six weeks, however, the cultures are kept until eight weeks. The patient is then re-examined by x-ray and his case is re-evaluated. Most of these are discharged with no clinical evidence of active tuberculosis. — Reprinted from *Tuberculosis Abstracts*, September, 1945

NOTE

On August 24, the Salem Tumor Clinic sponsored a teaching clinic at the Salem Hospital. Dr. Ira T. Nathanson, of

Boston, gave a talk entitled "Head and Neck Cancer", this was attended by staff members of the Salem Hospital, several visiting physicians from surrounding communities and a number of nurses.

CORRESPONDENCE

DR. RUSHMORE RETIRED AS DEAN

To the Editor: I should like to inform the medical profession, through the courtesy of the *Journal*, that I am no longer dean of the School of Medicine, Middlesex University, having been retired recently by vote of the Trustees of the University, which vote was worded to take effect immediately. I am devoting myself to the practice of obstetrics and gynecology.

STEPHEN RUSHMORE, M.D.

MEDICAL AND PUBLIC-HEALTH PERSONNEL NEEDED IN CHINA

To the Editor: The Chinese Government has requested UNRRA to provide, as soon as possible, some two hundred field personnel of the following categories to strengthen the available Chinese personnel. Such personnel will be required to head the respective services in hospitals of 100 to 250 beds, which will be established in areas recently liberated from the Japanese.

General surgeons
Orthopedic surgeons
Genitourinary surgeons
Gynecologists and obstetricians
General physicians
Dermatologists and syphilologists
Ophthalmologists
Otolaryngologists
Radiologists
Dentists
Pediatricians
Laboratory technicians
X-ray technicians
Sanitary engineers
Public-health engineers
Public-health nurses
Clinical nurses

General practitioners with some specialist experience will be acceptable. Candidates should be under fifty-five years of age and in good physical condition.

Will those interested please write to me at UNRRA, 1344 Connecticut Avenue, N.W., Washington 25, D.C.

Szeming Sze, M.D., Chief
Far East Section, Health Division

United Nations Relief and
Rehabilitation Administration
1344 Connecticut Avenue, N.W.
Washington 25, D.C.

NOTICES

ANNOUNCEMENTS

Dr. Charles P. Sheldon announces the opening of an office at 270 Commonwealth Avenue, Boston.

Dr. Theodore L. Badger, who has recently returned from overseas duty with the Army of the United States, announces the reopening of his office at 264 Beacon Street, Boston, for the practice of medicine, particularly as it concerns diseases of the lungs.

Dr. Paul L. Sandi announces the removal of his office from 204 Hanover Street to 636 Beacon Street, Boston.

(Notices continued on page xxxi)

On the 3rd day of meningococcemia the patient complained for the first time of constant soreness in the neighborhood of the ensiform cartilage, accompanied by a sharp pain between the lower sternum on deep inspiration, occasionally radiating to the left shoulder. A loud pericardial friction rub was heard over the entire precordium. An electrocardiogram revealed elevation of ST₂, with inversion of T₃ and moderate right-axis deviation. On the 5th day of the disease, the pericardial rub was less pronounced. Ten cubic centimeters of serofibrinous fluid was removed from the pericardial sac and

He was hospitalized on May 12, at which time x-ray examination revealed pneumonia involving the right lower lobe. Despite adequate doses of sulfadiazine, the process spread, until it involved all three lobes on the right. Sulfonamides were stopped on May 19, at which time the patient developed right-sided pleurisy. On the following day 300 cc. of cloudy, straw-colored fluid was removed from the right pleural space. Smear and culture of this fluid showed a gram-positive diplococcus culturally similar to pneumococcus. No typing was done. On May 22, penicillin therapy was instituted, a total

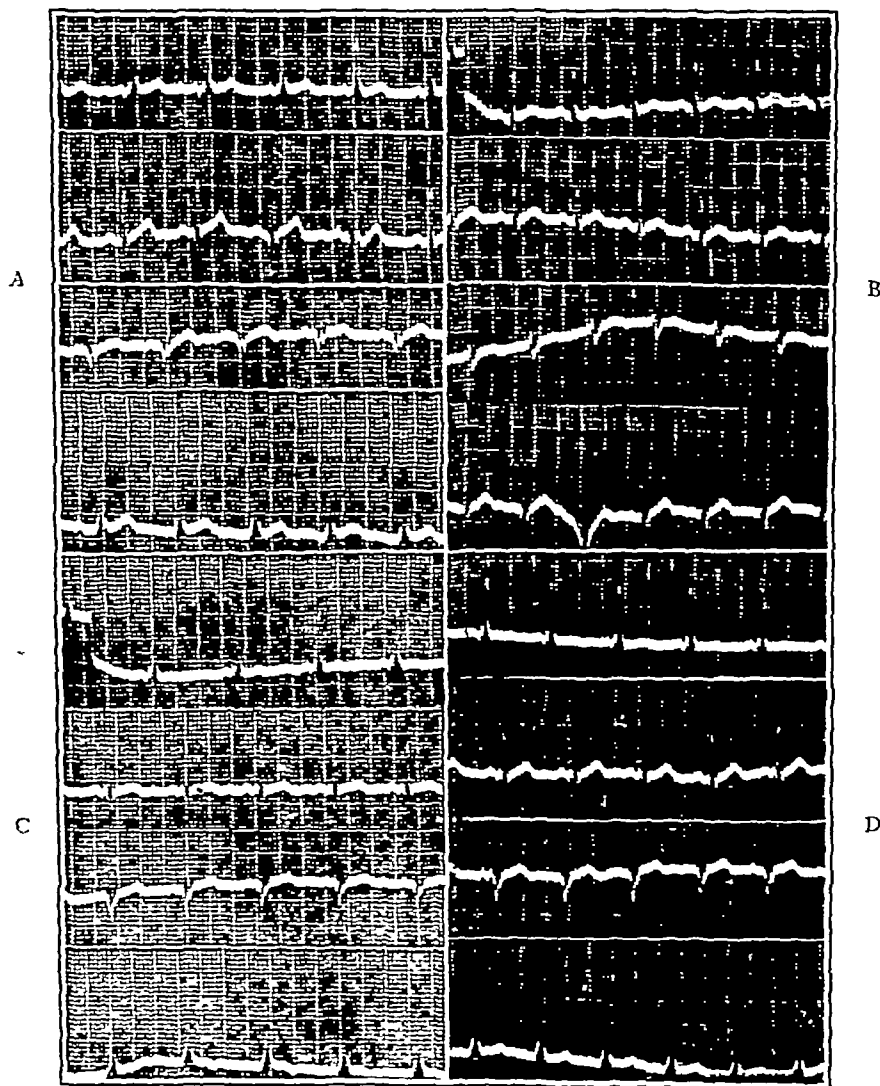


FIGURE 2 Electrocardiograms in Case 1

A was taken on the first day of disease, B on the tenth day, C on the twenty-ninth day, and D on the forty-first day

30,000 units of penicillin was instilled intrapericardially. At the same time 10 cc. of similar fluid was withdrawn from the left pleural space. The pleural fluid showed 7600 white cells per cubic centimeter, with 93 per cent polymorphonuclear cells. Culture of the fluid was sterile. The pericardial rub persisted until the 19th day. Clinical recovery was slow but uneventful. At the present time the patient is asymptomatic.

CASE 3 (Fig 4) This 25-year-old soldier was well until May 8 1944 when he developed fever, chills, pain in the right chest and a cough productive of blood-tinged sputum.

of 1,730,000 units being given in the next 16 days. On the same day excessive dyspnea and tachycardia were noted for the first time, and by May 25 a typical pericardial friction rub was heard over the entire precordium and persisted for 7 days. At that time, the temperature, which had been resolving by lysis, rose to 101.5°F. By June 6 it was normal, and convalescence from that point was uneventful.

Electrocardiograms made on May 24, the 2nd day after the onset of symptoms of pericarditis, showed no elevation of RS-T segments or alterations in T waves. X-ray examination revealed a moderate, diffuse enlargement of the cardiac silhouette. On May 29, the cardiac silhouette had increased

tioned the tamponade theory of the production of electrocardiographic changes in acute pericarditis, believing that the subepicardial myocarditis was a satisfactory explanation of the alterations. It was their impression that the most characteristic acute change in pericarditis was an elevation of the RS-T segment and an exaggeration of the T waves in the limb leads. This is followed by a return of the RS-T segments to normal, with a progressive lowering of the T waves, often proceeding to actual negativity. They did not observe elevations of the RS-T segments in tuberculous pericarditis.

As regards the electrocardiographic changes in rheumatic pericarditis, there is little in the literature. Winternitz and Langendorf¹⁰ reported their observations in 18 cases. Inasmuch as rheumatic pericarditis has often been considered to occur as an extension of myocarditis, there should be a sequence of events different from that seen in infectious pericarditis. Winternitz and Langendorf did not find this to be true, and their cases of rheumatic origin behaved exactly like those arising from other causes. In 8 of the cases in which they were able to follow the course of the disease completely, the tracings between the fifth and thirteenth weeks went through the stage of inversion of the T wave to restitution of a normal appearance.

MATERIAL

This series includes 8 cases of acute pericarditis. Six of these patients were followed in this hospital during all or part of the acute disease, and the other 2 were transferred here for convalescent care and disposition. The patients were men between the ages of twenty-two and twenty-seven. Six were Whites and two were Negroes. There were no deaths in the series during the time under observation at this hospital.

Etiologically the causative organism was demonstrated satisfactorily in 3 cases (it was the tubercle bacillus in 1 case, a meningococcus in 1 and a pneumococcus in 1). In 5 cases, the clinical course established strong presumptive evidence as to etiology, with a probable tuberculous origin in 2 cases and a probable rheumatic one in 3.

METHOD OF STUDY

A graph was devised to correlate several features. The so-called "heart size" recorded was the greatest transverse diameter, measured in centimeters on the standard 72-inch roentgenogram. The sum of the T waves in the four leads was determined algebraically and charted in millimeters. The elevations of the RS-T segment in the four leads were added and also charted in millimeters. The temperature was the highest recorded each day. The period of time that the friction rub was heard was charted. The electrocardiograms were made with the three standard limb leads and a precordial lead (Lead CF₄).

CASE REPORTS

CASE 1 (Fig 1) This 23-year-old soldier was admitted for treatment of a traumatic amputation of the left leg. The wound was clean and almost completely healed at the time of admission. While in the hospital, on April 10, 1944, he developed left pleurisy with effusion. Six hundred and seventy-five cubic centimeters of straw-colored fluid was removed from the left pleural space on April 19. Some of this fluid was injected into a guinea pig, which developed typical generalized lesions of tuberculosis within 6 weeks. The patient

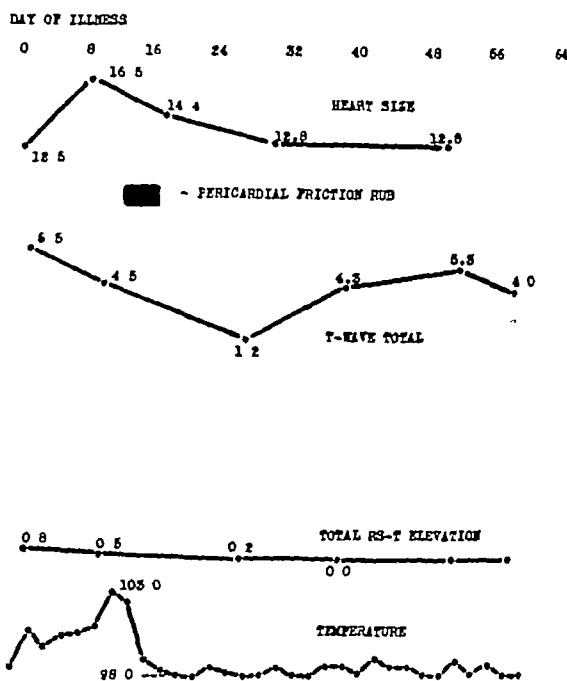


FIGURE 1 Graph of Findings in Case 1

required no further thoracenteses and improved rapidly, becoming afebrile by May 18.

On the evening of June 8, he developed nonradiating substernal pain, which was increased by respiratory movements. The temperature rose to 101.2°F. Pericarditis was suspected, but electrocardiograms taken at that time were normal except for a slight RS-T elevation (Fig 2A). On June 18, the 10th day of the pericarditis, the electrocardiograms revealed some reduction in the RS-T elevation, with a general reduction in QRS voltage in all leads. The T waves in the limb leads were of lower voltage than in previous electrocardiograms (Fig 2B). X-ray films taken 2 days earlier had demonstrated an increase in the cardiac shadow, with a globular configuration suggestive of pericarditis. A to-and-fro friction rub was heard over the precordium. On July 7, the electrocardiograms showed an isoelectric T₁ and an inverted T₂. T₂ was lower than in previous electrocardiograms (Fig 2C). X-ray examination on July 10 revealed a normal cardiac shadow. By July 19, the electrocardiogram showed a slightly upright T₁ and an upright T₂. T₂ and T₃ had returned to normal (Fig 2D). X-ray examination of the chest on July 31 showed no change.

CASE 2 (Fig 3) On March 16, 1944, this 24-year-old soldier was admitted to a hospital overseas in a state of profound shock. He was conscious and stated that he had had fever, headache, nausea and vomiting for 24 hours. His neck was stiff. A lumbar puncture done on admission produced grossly purulent fluid containing meningococci on smear and culture. Ten thousand units of penicillin was given intrathecally, followed by 50,000 units intravenously and 50,000 intramuscularly. The patient was also given 5 gm of sodium sulfadiazine intravenously and thereafter was carried on large doses of sulfadiazine and penicillin.

decreased slightly (Fig 6D), but the cardiac silhouette was unchanged. Electrocardiograms made on the 86th, 89th and 93rd days of disease showed no essential change in the T wave, and the x-ray films were likewise unchanged. The patient was still running a low-grade fever and was discharged to a Veterans' Facility for further care.

CASE 5 This 24-year-old soldier was well until June 15, 1943, at which time he was admitted to a hospital overseas.

Three days later he developed fever, with a hacking cough, substernal pain and chills. He was readmitted on November 15 with fever, leukocytosis and severe anterior chest pain. On November 18, a chest x-ray film revealed marked increase in the cardiac silhouette, and the pericardial friction rub was heard in the 4th left interspace. The patient was transferred to another hospital on November 25, the 13th day of symptoms referable to pericarditis, where electrocardiograms showed inversion of the T waves in all leads.

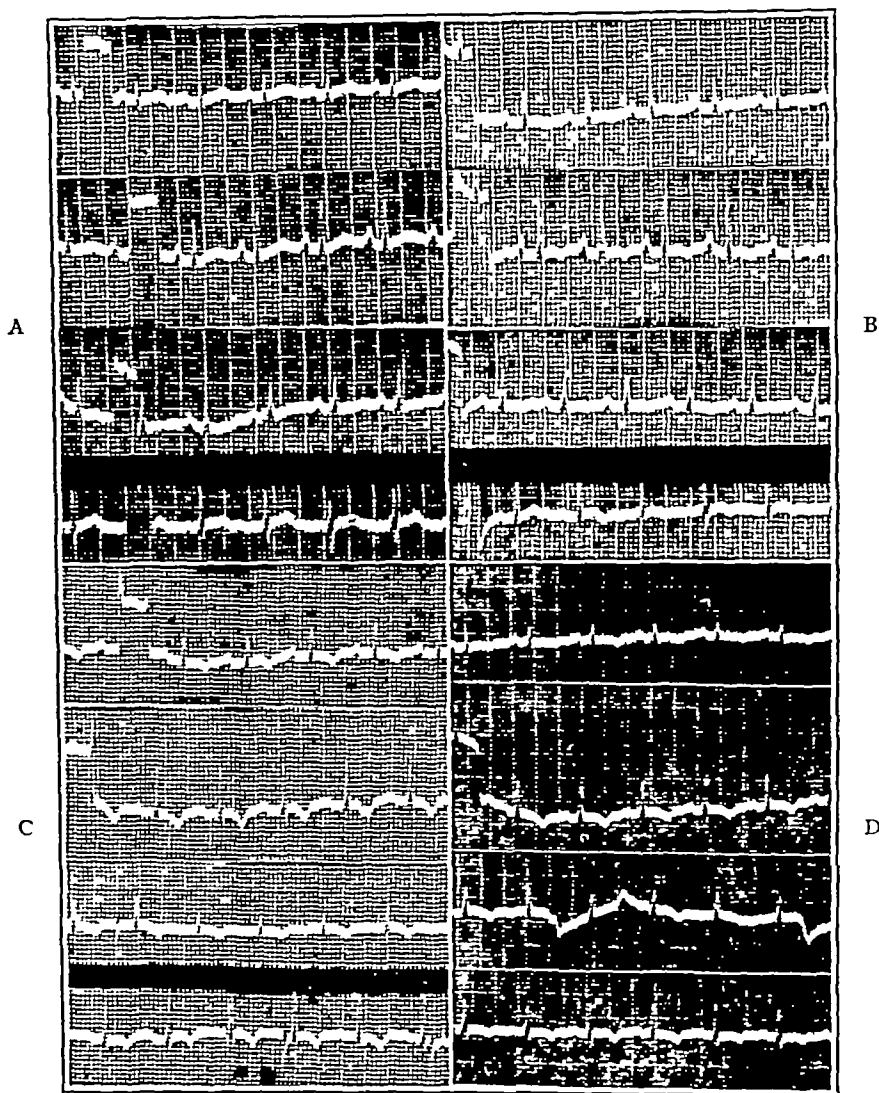


FIGURE 6 Electrocardiograms in Case 4

A was taken on the sixth day of disease, B on the twelfth day, C on the thirty-sixth day and D on the sixty-third day.

with complaints of fever, substernal pain, tachycardia and generalized aching. Electrocardiograms were not available, but he had no pericardial friction rub and chest x-ray films showed no enlargement of the cardiac silhouette. He continued to have an elevated temperature for a month but did not have true migrating polyarticular disease. The tachycardia recurred at times, and on one occasion a diagnosis of paroxysmal tachycardia was made. He was finally released from this hospital on September 20, but was readmitted on October 27 with complaints of substernal distress and dyspnea. Again the physical and laboratory studies were negative but no electrocardiograms were taken. He was discharged on November 9.

A chest x-ray film showed no change. On December 1 the electrocardiogram was unchanged but by December 6 there was considerable increase in negative deflection of all T waves, with an ST pattern in Leads 1 and 2 suggesting a so-called "coronary T." At that time x-ray examination showed marked reduction in the size of the cardiac shadow. On January 13, the 62nd day of disease the heart was still smaller and the T waves were not so deep. By February 8 the heart was of normal size but the T waves had not changed except that T₁ had become diphasic. On March 22 T₁ was upright, and the other T waves were diphasic. On June 16 the cardiac silhouette was still normal and T₂ was normal. T₁ low but upright and T₃ and T₄ slightly inverted. The

markedly in size, but the electrocardiograms were unchanged. By June 3 there was definite diminution in the size of the

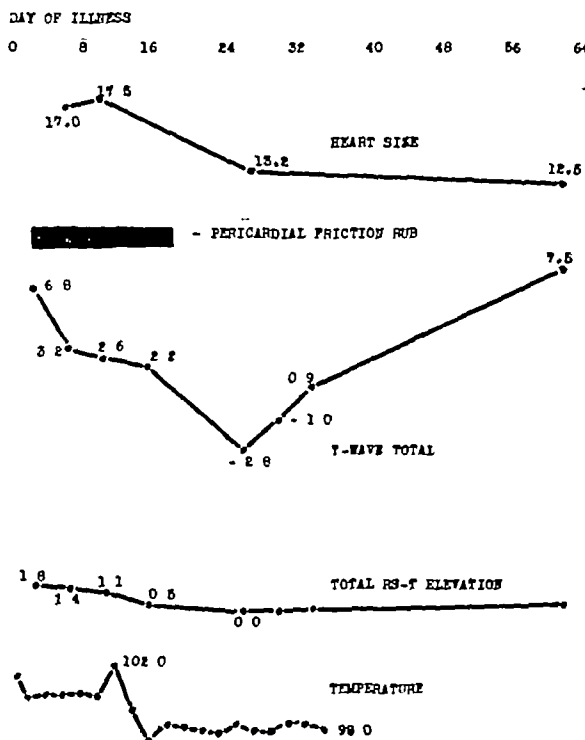


FIGURE 3 Graph of Findings in Case 2

cardiac shadow but no change had occurred in the electrocardiograms. X-ray examination of the chest on June 8

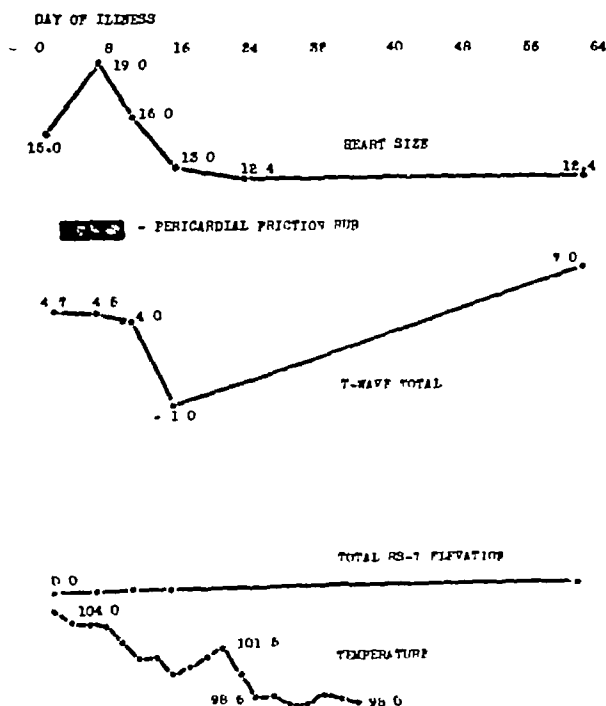


FIGURE 4 Graph of Findings in Case 3

revealed reduction of the cardiac silhouette to normal. Electrocardiograms made on that day, however, showed for

the first time a diphasic T_1 , inverted T_2 and T_4 and an isoelectric T_3 . On July 26, the 65th day of the pericarditis, both chest x-ray film and electrocardiogram were normal.

CASE 4 (Fig 5) This 27-year-old soldier was well until December, 1943, when he developed "flu" in England. He recovered after a week and was well until March, 1944, when he had an attack of so-called "primary atypical pneumonia."

On May 8, the patient developed cough, fever and pain in the left chest, aggravated by deep breathing. The next day, beginning to raise much yellow sputum, he was put on sulfadiazine, which was continued for 5 days. On May 14, he was admitted to the hospital with a high temperature. There were rales at both lung bases, the liver was enlarged, and the neck veins were distended. On May 17, mercurial diuretics were tried, with moderate success. During that time the liver increased rapidly in size and became tender.

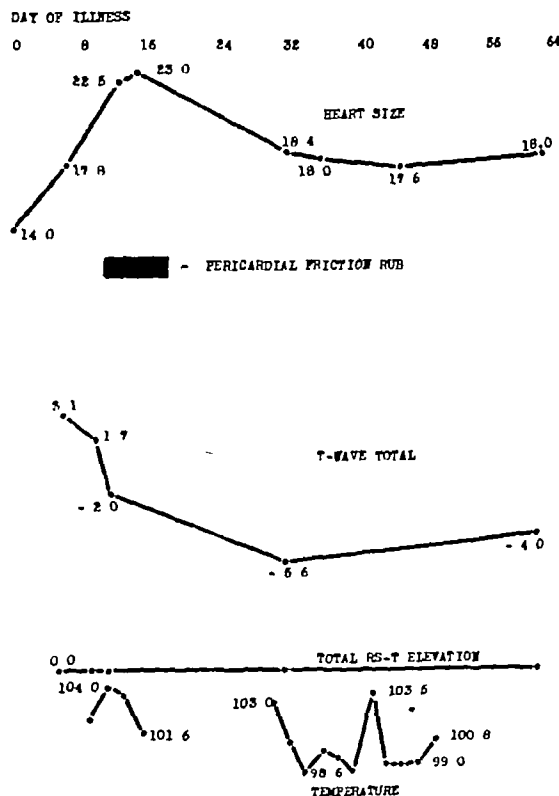


FIGURE 5 Graph of Findings in Case 4

On May 19, a pericardial tap was performed and 80 cc of clear yellow fluid was removed. The fluid formed a pellicle within a few minutes and clotted within an hour. No organisms could be demonstrated on smear or culture. After pericardiocentesis, there was relief of dyspnea and the previously observed pulsus paradoxus disappeared. On May 20, a pericardial friction rub was heard for the first time, persisting until May 26. During the next month treatment consisted of bed rest and salicylates, which reduced the fever somewhat. There was at no time any evidence of joint involvement. On July 18, the condition was unchanged except for pain in the right chest and a friction rub over this area. During the next week friction rubs were heard over both pleural areas. Chest x-ray films revealed extensive pleural thickening but no free fluid.

On May 14, a chest x-ray film revealed moderate enlargement of the heart, but the electrocardiogram was normal (Fig 6A). By May 20, roentgenograms showed a marked increase in the size of the heart and electrocardiograms showed slight inversion of T_1 , T_2 and T_4 , with a diphasic T_3 (Fig 6B). On June 13, the heart had decreased in size but the T-wave inversion had increased (Fig 6C). On July 10, the 63rd day of the disease, the total T wave inversion had

CASE 8 (Fig 9) This 23-year-old soldier was well until January, 1944, at which time he began to lose weight and develop pain in the left chest. A diagnosis of fibrinous pleuritis was made, and he continued to have distress in the chest. On April 25, he was admitted to a hospital, where he was found to have left pleurisy with effusion. A diagnostic

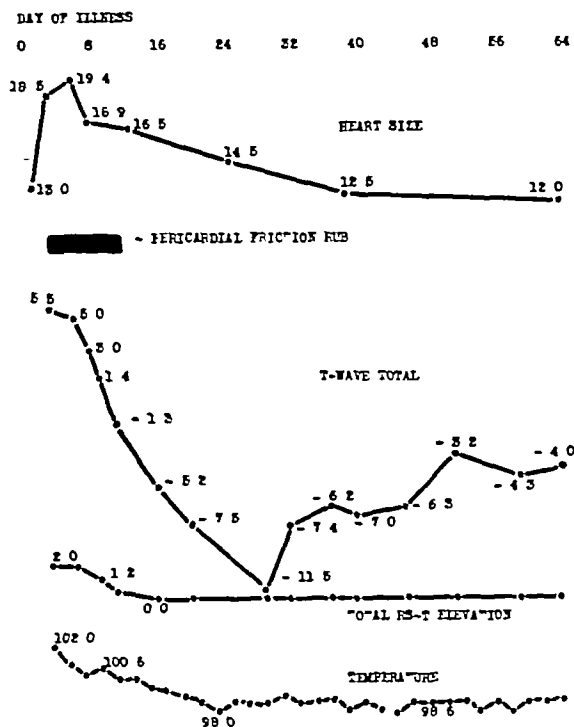


FIGURE 9 Graph of Findings in Case 8

thoracentesis was done, with removal of 25 cc. of slightly turbid fluid. Some of this was injected into a guinea pig, but the report of this examination is not available. When the patient arrived at this hospital on June 30, x-ray examination showed a diffuse clouding of the lower two thirds of the left lung field. He was afebrile and complained only of some distress in the left chest on deep breathing.

Progress was uneventful until August 1 when the patient developed pain in the left shoulder and the left side of the neck, accompanied by a feeling of substernal pressure. The next day the temperature was 99.8°F, and physical examination revealed a pericardial friction rub in the 2nd and 3rd interspaces to the left of the midline. The following day the temperature reached 102°F. Electrocardiograms showed some elevation of RS-T₂ but nothing else. Chest x-ray examination revealed a marked increase in the transverse diameter of the heart. The pericardial friction rub persisted for 9 days. The temperature went down slowly by lysis becoming normal on the 20th day and remaining normal thereafter. The heart was largest on the 5th day, thereafter gradually returning to normal, reaching its original size on the 38th day. Progress electrocardiograms showed progressively increasing negativity of the T waves, reaching a maximum on the 25th day. The white-cell counts throughout the acute illness varied between 6700 and 8100 with 65 per cent polymorphonuclear cells. The sedimentation rate was 42 mm per hour on the 2nd day, 27 mm on the 7th, 38 mm on the 12th, 34 mm on the 15th, 26 mm on the 22nd, 11 mm on the 31st, 11 mm on the 38th, and 12 mm on the 50th. Improvement was uneventful.

DISCUSSION OF CHARTS

It is to be noted that Cases 1, 2 and 3, although representing three different etiologic agents, present a similar picture (Figs 1, 3 and 4) when recorded by

this graphic method. In all of them, the heart increased rapidly in size, reaching its maximum by the tenth day. At the time of maximum change in heart size there was little or no change in the electrocardiogram, although in Cases 1 and 2 some elevation of the RS-T segment had occurred. In all three the maximum T-wave inversion occurred after the heart had returned to its original size. This is a significant point in diagnosis and will be emphasized later.

T-wave inversion sometimes occurs after the temperature has returned to normal and the patient is clinically well. This is well illustrated in Cases 1 and 2 and may also have been true in Case 3, but there was a long interval during which time no electrocardiograms were obtained.

Of special significance is the fact that the T-wave total in Case 1 was positive throughout. In other words, no single electrocardiogram in this case (Fig 2) can be considered typical of pericarditis. It was only by repeated examinations that the characteristic picture could be demonstrated on a graphic chart. This point is also worthy of repeated emphasis. The diagnosis of pericarditis by electrocardiograms is frequently impossible without repeated examinations.

In Case 4 (Fig 5), the patient, who presumably had a tuberculous polyserositis, continued to run an irregular fever after two months of illness. The electrocardiogram and chest x-ray picture remained unchanged during the time that he was at this hospital. The graph is important in again demonstrating that the maximum T-wave inversion occurs after the heart has returned to a normal or nearly normal size. Also to be emphasized is the fact that the T waves remained inverted as long as this patient was under observation, during which time the pericarditis continued to be active.

A graph was not made in Case 5 because the x-ray films were not available, but this case is of interest in that the T waves remained low for nine months, during which time there was clinical evidence of activity of the rheumatic process.

The patient in Case 6 had a severe rheumatic pericarditis, and it may be seen that the heart had reached its maximum size and was returning toward normal before the T waves reached their lowest point (Fig 7). The picture is similar to that in Figures 1, 3 and 4, except that the time intervals are much longer.

In Figure 8, it may be seen that the patient (Case 7) was the only one who showed maximum T-wave inversion before the heart had reached its greatest size. Also of interest in this case is the fact that an early T-wave inversion was followed by nearly isoelectric waves and then by more marked inversion. Although occasionally such rapidity of electrocardiographic alteration is seen in acute myocarditis secondary to rheumatic fever or myocardial infarction, it was not seen in the other cases.

patient continued to have an elevated temperature, with daily peaks of 99.8 to 100.4°F, for another month (Progress was not recorded graphically because none of the overseas x-ray films were obtainable)

At the time of discharge, over 9 months after onset, he was still running a low-grade fever, with low total T wave deflection, and was transferred to a Veterans' Facility for further care.

CASE 6 (Fig 7) This 22-year-old soldier had a severe renal reaction following the giving of sulfathiazole in May, 1942, for treatment of a local infection in the right hand fol-

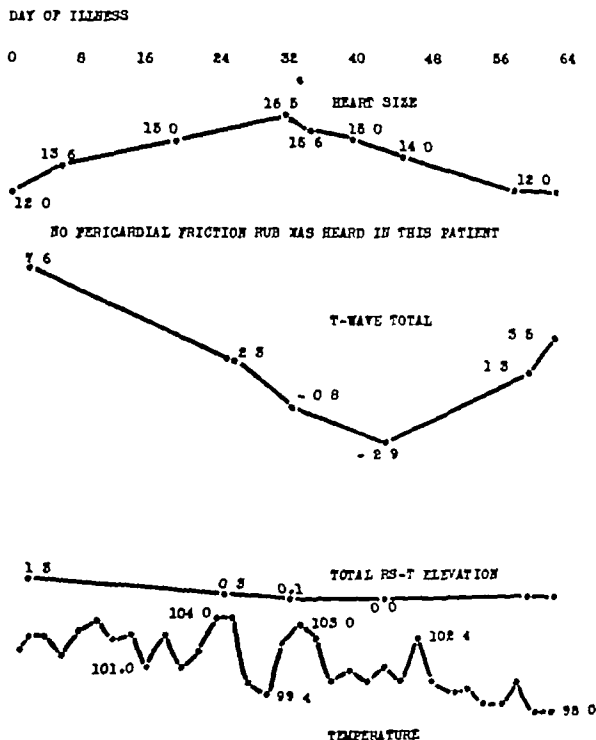


FIGURE 7 Graph of Findings in Case 6

lowing an injury. He was well following this until April 24, 1944, at which time he developed a sore throat, followed within 48 hours by severe aching pain in the legs. He was treated with large doses of intravenous sodium sulfadiazine, and within 24 hours had developed grossly bloody urine and a temperature of 105.6°F. The sulfonamide was discontinued, but the patient continued to run a septic fever, with peaks over 104.0°F daily. The white-cell count ranged between 8600 and 11,950, and all studies, including blood cultures, agglutination tests, stool and urine cultures and x-ray films of the chest, were normal.

On May 6, the patient complained of severe pain in the precordium. An electrocardiogram on May 8 showed an elevated RS-T segment in Leads 1 and 2 without T wave changes. X-ray examination on May 16, the 10th day of symptoms referable to the pericardium, showed no increase in the size of the heart. No electrocardiograms were available from May 8 until May 31, when the T waves in Lead 4 were inverted and those in the limb leads were lower than before but still upright. On June 8, x-ray examination revealed a marked increase in the size of the heart. An electrocardiogram on that date showed little further change, except for slightly lower T waves in the limb leads. On June 12, there was no change in the electrocardiogram or x-ray film. During that time the patient had shifting joint pains without marked swelling and a spiking fever, with the peaks less out marked severe chills, followed by an increase in temperature. On May 9, he had pain in the left side of the chest and a definite pleural fric-

tion rub was heard, but fluid did not appear. Six hundred and ninety thousand units of penicillin was given, without relief, but salicylates were not tried. Studies continued to be negative except for the chest x-ray film and electrocardiogram and an increased white-cell count, which reached 35,150 on one occasion, with 85 per cent polymorphonuclear cells. On transfer to this hospital on June 20, the cardiac silhouette was still enlarged and the electrocardiogram showed inversion of T waves in all four leads. The patient complained of severe joint distress without marked swelling, but had no pleural or pericardial friction rubs. The temperature was still high, but subsided within 48 hours after the patient began to receive 4 gm of aspirin daily. On July 11, a chest x-ray film revealed a normal-sized heart. Electrocardiograms showed upright T waves in all leads.

CASE 7 (Fig 8) This 26-year-old soldier was well until May 26, 1944, when he first noticed stiffness of the joints. The following day he developed precordial pain, radiating to the left side of his chest and aggravated by deep breathing. He began to cough, raising moderate amounts of creamy sputum without blood. He was admitted to the hospital, where the temperature was found to be 101.4°F. For the next 4 days it never dropped below 100. The pulse rose to a level of 90 to 120. On admission to the hospital he was given 6 gm of sulfadiazine, and thereafter received 1 gm every 4 hours until June 10. The blood level of the drug rose as high as 21 mg per 100 cc, but the clinical symptoms were unaffected.

On June 1, the patient developed severe joint pains, with redness and swelling of the involved joints. The right knee was particularly severely involved, and was tapped twice, with removal of 30 cc of turbid fluid, negative to culture.

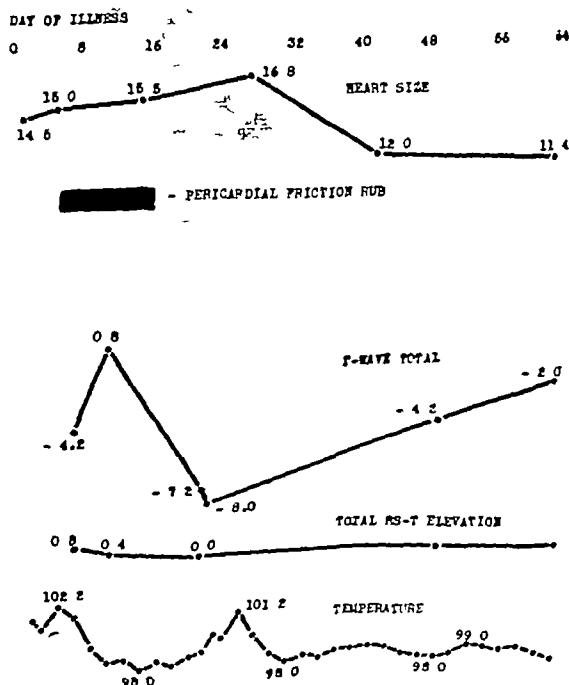


FIGURE 8 Graph of Findings in Case 7

He was started on salicylate therapy on June 10, and the clinical response to 1 gm of aspirin four times daily was dramatic.

On June 2, a pericardial friction rub was heard for the first time. The precordial aching that had been the first symptom was aggravated and persisted with the rub until June 13. Convalescence was uneventful except for the persistence of electrocardiographic alterations.

total T-wave deflection, total elevation of the RS-T segment, pericardial friction rub and temperature. Elevation of the RS-T segment occurred early, was usually slight and disappeared rapidly. The T-wave total began to decrease soon after onset of the disease, but did not reach its lowest point for about four weeks. Judging from the cases observed, there is no significant electrocardiographic difference in the pericarditis caused by rheumatic fever, tuberculosis or pneumococcal or meningococcal infection.

This graphic method of correlating clinical observations in acute pericarditis emphasizes several points. The diagnosis can seldom be made from a single electrocardiogram. In some of these cases the correct diagnosis was delayed for days or weeks because the typical picture did not appear. The T waves may never become isoelectric or inverted, yet a careful analysis of their total deviation may demonstrate significant alterations. Total inversion is a late finding, usually occurring after the heart has returned to normal size and the fever has subsided. The T waves, however, begin to lose amplitude early in the course of the disease, and it is this progressive change that is most important in early

diagnosis. It is not necessary to wait until total inversion has occurred to diagnose pericarditis. By careful daily measurement of the T waves, progressive decrease in amplitude can be detected.

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FALSE-POSITIVE HINTON REACTIONS FOLLOWING CHICKEN POX*

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BOSTON

THE evaluation of the specificity of the various tests for the serologic diagnosis of syphilis has gone through two phases. At one time both the complement-fixation and flocculation tests were considered to be so highly specific that some states accepted them as legal proof of a previous or existing syphilitic infection. During the last fifteen years there has been a re-evaluation of these tests and an increasing appreciation of the fact that certain non-syphilitic conditions are capable of producing biologic false-positive reactions. Furthermore, the possibility of technical false-positive reactions has been repeatedly demonstrated by the interstate serologic surveys conducted by the Committee on Evaluation of Serodiagnostic Tests for Syphilis of the United States Public Health Service.¹

The diseases already described as being able to produce false-positive reactions include yaws, pinta, bejel, leprosy, malaria, infectious mononucleosis, vaccinia (variola), tuberculosis, atypical pneumonia, disseminated lupus erythematosus, rat-bite fever, relapsing fever, herpes genitalis, miscellaneous upper respiratory infections, measles, typhus fever, typhoid fever, subacute bacterial endocarditis, Weil's disease,

Vincent's angina, diphtheria, glanders, rheumatic fever, mumps, infectious hepatitis, chancroid, lymphogranuloma inguinale, scarlet fever, leishmaniasis, kala azar, trypanosomiasis, tularemia, Rocky Mountain spotted fever, leukemia, pellagra, psoriasis, coronary thrombosis, diabetes mellitus, eclampsia, lead poisoning and acute alcoholism. Other conditions include ether anesthesia, hyperglobulinemia, sulfonamide therapy, menstruation, pregnancy, malignancy and injections of horse serum. Kolmer¹ has recently published an excellent review of the problem, and Davis² has evaluated the literature on false-positive tests. The latter believes that the ability of a number of the above listed conditions to produce false-positive reactions has not been adequately demonstrated.

During the last one and a half years we have had occasion to observe the occurrence of transient false-positive Hinton reactions in patients convalescent from chicken pox. A review of the literature fails to reveal any previous observation of this nature except that of Gunn,³ who in 1930 reported one questionably positive and three definitely positive Wassermann reactions in convalescent serums from 25 cases of chicken pox. No flocculation tests were performed. Since adequate standardization had not yet become widespread prior to 1930,² Gunn's results are open to reasonable question.

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we have studied or in those reported in the literature, except in a single case reported by Fuller and Quinlan.¹¹ It is possible that the primary inversion was caused by rapidly accumulating fluid in a pericardial sac that could not stretch. This suggestion is given some support by the fact that the heart never became particularly large, despite the severe degree of T-wave inversion. On the other hand, no evidence of the presence of cardiac tamponade appeared at that time, so that no proof of markedly elevated intrapericardial pressure can be found. The patient was seen at this hospital on about the sixtieth day of his illness. At that time, as may be seen, he was afebrile and the heart had returned to normal size, but he still had T-wave inversion. The sedimentation rate and white-cell count were normal. The T waves became upright within four weeks.

The patient in Case 8 was followed in this hospital throughout his entire course. It may be seen that the x-ray and electrocardiographic changes followed the typical pattern for two months (Fig 9). The sedimentation rate was normal by the thirty-first day and the heart was normal by the thirty-eighth day. Electrocardiograms showed a rapidly progressive increase in the T-wave inversion until the twenty-ninth day. This inversion was the most marked in this series of cases, totaling 11.5 mm. From the twenty-ninth to the fifty-first day it decreased. From that point it remained unchanged, and at the time this paper was written, on the 73rd day of the disease, the total inversion was the same. The temperature, white-cell count and sedimentation rate were normal and the patient was asymptomatic.

DISCUSSION OF OBSERVED CHANGES

The first change generally referred to in the textbooks is elevation of the RS-T segment. This was noted in 5 of the 7 cases presented but was never extreme, the highest being 2.0 mm (Case 8). It was a transient change, persisting from sixteen to thirty days. From an etiologic point of view, it was noted in all three of the cases of rheumatic pericarditis and in the single case of meningococcal involvement. It was also present, although minimal, in one of the 2 tuberculous cases and was absent in the patient with pneumococcal disease. It should be carefully searched for in every suspected case of pericardial inflammation, since these graphs clearly show that it is the first demonstrable change. It may, however, be found in normal persons, and serial electrocardiograms are often necessary before an accurate diagnosis can be established.

In this series, the maximum T-wave inversion came between the sixteenth and the forty-third day of disease, with an average of twenty-seven days. Considered according to etiology the figures are sixteen days for the pneumococcal case, twenty-five for the meningococcal, twenty-nine for the

tuberculous and thirty-one days for the rheumatic. This time interval should be emphasized, inasmuch as a patient with acute pericarditis may die long before diagnostic T-wave inversion appears.

Sometimes the T-wave inversion does not involve all four leads, and occasionally only one or two are inverted. There is usually, however, some reduction in total T-wave deflection, as is well illustrated in Case 1. This can be shown only by careful measurements in serial electrocardiograms.

In 5 cases, the T waves returned to normal while the patient was under observation. This occurred in forty days in the pneumococcal case, in forty-eight in the meningococcal case, in fifty-two in the tuberculous case, and in an average of seventy-seven in the rheumatic cases. The average for the 5 cases was fifty-nine days. In one rheumatic case (Case 5) the T waves remained low over nine months, and in another (Case 8) they were still inverted after ten weeks. In the patient with tuberculous polyserositis, they were inverted when he was transferred, over three months after onset.

These observations vary somewhat from those of Vander Veer and Norris,⁸ who found that the electrocardiogram returned to normal even though the active pericardial infection was persisting and the pericardial effusion increasing.

We are not certain about the significance of persistent T-wave inversion long after the temperature, pulse, chest x-ray film, white-cell count and sedimentation rate have become normal. It is possible that these changes are similar to those seen in cases of myocardial infarction, in which T-wave deviations sometimes persist for many months after the acute incident. In our opinion, however, persistent inversion must be regarded with caution, and it has therefore been our practice to restrict the activities of the patient until the T waves return to normal.

There was no consistent variation in QRS amplitude, although a lowered total deflection has been mentioned as one of the diagnostic signs in acute pericarditis.

In this series, the heart reached its maximum size rapidly. Wolff¹² has asserted that the increase in cardiac silhouette that occurs in acute pericarditis may be due to dilatation rather than to pericardial fluid. In this series, Cases 1 and 4 received pericardial taps to demonstrate the presence of fluid. In all the others there was a roentgenologic diagnosis of pericarditis with effusion.

In this series the pericardial friction rub appeared from the second to the thirteenth day of disease. It was present for four to sixteen days, with an average of nine days. In only 1 case was no rub heard at any time.

SUMMARY AND CONCLUSIONS

In 8 cases of acute pericarditis observed during a period of three months at Battey General Hospital, a graph was devised to correlate heart size,

be followed serologically and without treatment for a period of three months, serologic tests being performed each two to four weeks. At the end of this period those in whom the serologic reaction has reverted to negative are discharged from observation as nonsyphilitic, those showing persistently positive tests are regarded as syphilitic, and those still showing conflicting serologic reactions are subjected to further study.

Moore et al⁵ have outlined a suggested clinical approach to the study of this type of case. Mahoney⁶ stresses the fact that a certain amount of disagreement in the findings of any two tests is to be anticipated, and observes that these discrepancies may be looked on as a shortcoming of the science of serology rather than as a limitation of an individual technic. That this discrepancy between tests cannot be relied on for the detection of false-positive reactions is brought out by Crawford and Ray's⁷ observation that 26 per cent of over 1000 cases considered to be syphilis showed positive Hinton and negative Wassermann reactions.

SUMMARY

Twenty-two unselected cases of chicken pox are presented, 5 of which exhibited transient false-

positive Hinton reactions for syphilis. In addition, 1 patient developed a transient positive Kahn reaction. No false-positive Wassermann reactions were obtained. The need for a critical approach to serodiagnosis is again emphasized.

We are indebted to Miss G O Stuart, of the Wassermann Laboratory, for performing the serologic tests and to Dr G N Hoefel for permission to use the clinical material at the New England Peabody Home for Crippled Children.

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MEDICAL PROGRESS

THE PARENTERAL USE OF VITAMIN PREPARATIONS (Concluded)*

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NIACIN

Niacin (nicotinic acid) is another water-soluble member of the vitamin B complex. In whole blood, its concentration varies between 0.3 and 0.9 mg per 100 cc, 90 per cent of this amount being present in the corpuscles as a constituent of co-enzymes I and II.⁷¹⁻⁷² The plasma content of niacin, apparently in the free form, ranges between 0.05 and 0.24 mg per 100 cc.^{72, 73}

When niacin is injected, its amide (nicotinamide, niacin amide) should be used to avoid the distressing flushing reactions that attend the parenteral administration of niacin itself. The injection of large doses of nicotinamide intravenously or intramuscularly is followed by a definite rise in the total niacin content of the blood, but the rise and its duration (one to four hours) are small in proportion to the dose given.⁷² Of the administered nicotinamide, some is probably methylated in the liver⁷⁴, but the metabolic fate of the major portion is unknown since the amount of niacin or its known

derivatives that can be recovered in the urine after the administration of a test dose usually does not exceed 10 per cent of that dose.^{73, 75}

Niacin itself is present in quite small quantities in human urine, and its urinary excretion does not increase appreciably after nicotinamide is given whether intravenously (200 mg.⁷⁶) or orally (500 mg.⁷⁷ and 50 mg.⁷⁸). A methylated nicotinamide derivative, variously identified as trigonelline,⁷⁶ fluorescent pigment F₂,⁷⁹ N-methyl nicotinamide^{74, 78-80} and nicotinamide methochloride,⁸¹ has, however, been identified in human urine. Since this derivative constitutes over 90 per cent of the known niacin products in the human urine,⁷⁸ and since many authorities (but not all⁷⁵) believe that its urinary excretion is an index of niacin stores, saturation tests have principally relied on the measurement of the methylated nicotinamide in the urine.

In normal subjects, 200 mg of nicotinamide, whether given orally or intravenously, was followed by an 18 to 30 per cent urinary recovery (as trigonelline) in the next twenty-four hours.⁷⁸ Doses of 500 mg were followed in a twelve-hour period by a 90-mg average excretion in normal adults and a 41-mg

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CLINICAL MATERIAL

The cases of chicken pox comprised in this study include 11 occurring in Harvard University students hospitalized at the Stillman Infirmary and 11 in children at the New England Peabody Home for Crippled Children. All bloods were carefully drawn and were delivered in person to the Massachusetts Wassermann Laboratory, and the tests were carried out by the same skilled technician, using undiluted serum. Wassermann, Hinton and Kahn tests were performed on each specimen. All but 1 of the patients who developed a positive Hinton reaction during convalescence were known to have had a negative reaction prior to the onset of their illness.

tuberculosis, the positive serologic reactions obtained in this case may not have been due to chicken pox. It is interesting to note, however, that the Hinton, Kahn and Wassermann reactions were negative in the 5 other cases of bone and joint tuberculosis included in this series.

The earliest positive reaction developed seven days after the onset of the eruption, and in 1 case persisted for fifty-one days. Within eighty-six days all the positive reactions had reverted to negative.

DISCUSSION

From this small series it is evident that positive Hinton reactions may be obtained following chicken

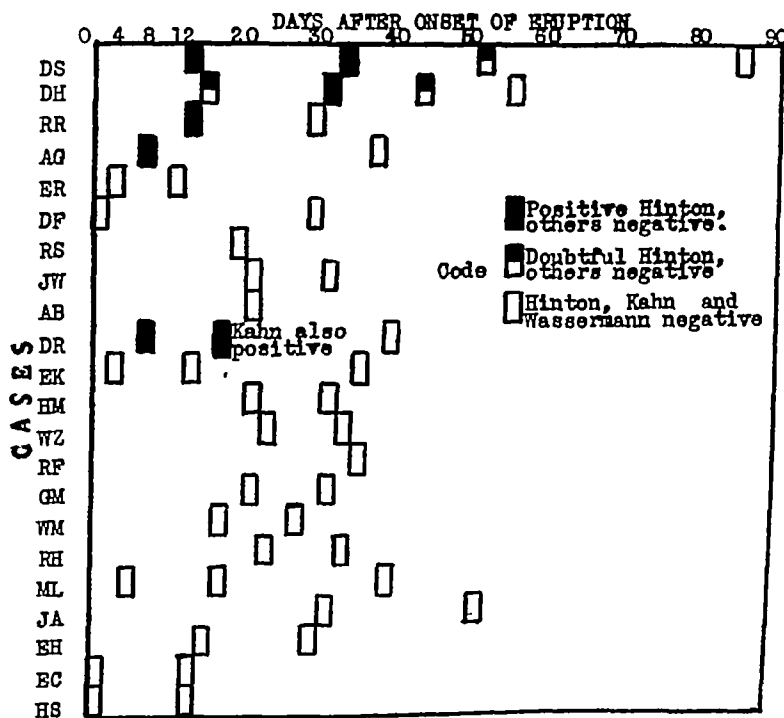


FIGURE 1

Those who developed positive reactions were followed at varying intervals until these became negative. Since the tests were performed in a well recognized serologic laboratory, the possibility of technical error was reduced to a minimum.

RESULTS

In Figure 1 are listed the results obtained on serums from 22 unselected convalescent cases of chicken pox. Five of these patients (22 per cent) developed positive Hinton reactions, and 1 showed a positive Kahn reaction as well. In no case was the Wassermann reaction positive. All but 1 of the patients who developed positive Hinton reactions were healthy adult males. The exception was a girl with tuberculosis of the spine. Since false-positive Hinton reactions have been reported in

pox, in 1 case there was a positive Kahn reaction. This series is obviously too small to reflect the true incidence of biologic false-positive reactions in this disease, but our results of 5 false-positive reactions in 22 cases tested (22 per cent) suggests that this reaction is not infrequent and is possibly as frequent as the false-positive reactions obtained in malaria (16 per cent) and after vaccination (12 per cent¹).

These results again emphasize the need for a critical approach to the results of serologic tests and careful evaluation of each case before the patient is subjected to the psychologic trauma of a diagnosis of syphilis and the physical trauma of antisyphilitic treatment. The present Army⁴ approach to this problem is as follows:

It is recommended that such individuals who have no conclusive history or clinical manifestations of syphilis

The short period of urine collection may have influenced these results, but the peak in the excretion passed before the end of the two-hour period, even in the oral tests⁸⁹

A pantothenic acid intake of 10 or 11 mg per day has been estimated to be a safe level for man^{8, 90} In adult dogs, large daily doses of calcium pantothenate (40 mg orally) seem to bring about enough storage of this substance so that the dogs can subsist for two or three months on a diet deficient in pantothenic acid⁹¹

Pyridoxin excretion in the urine contrasts with pantothenic acid in that the excretion of the former appears to be independent of the route of administration An oral dose of 100 mg of pyridoxin in man is followed by a 75 per cent recovery in the urine four hours later⁹² After an intravenous dose of 50 mg, the urinary recovery in one hour lies between 8 and 9 per cent,^{92, 93} a figure that is practically identical with the results of the oral test In spite of the apparent ability of the body to "take up" injected pyridoxin, one should be cautious in concluding that the huge doses that have been recommended for certain disorders such as irradiation sickness or agranulocytosis are actually economical and rational from the viewpoint of the body's ability to utilize this substance It should be recalled that the assay for pyridoxin and knowledge concerning its metabolism and that of related compounds leave considerable room for improvement⁸

On the basis of indirect evidence, man's "requirement" for pyridoxin has been set at 15 mg per day⁹⁰

Although the role of pyridoxin and pantothenic acid in human nutrition is still uncertain, there is little doubt that vitamin B complex contains factors essential for man's health Chiefly on the basis of animal experiments, vitamin-like activity has been ascribed to various substances, of which biotin, inositol, choline, para-aminobenzoic acid and folic acid (*Lactobacillus casei* factor) are among the better known⁹⁴ Most of these factors are untried entities so far as human nutrition is concerned, but some of them, or others as yet unknown, must account for the fact that sources of vitamin B complex, such as brewer's yeast, supply man with nutritious principles that are lacking from pure preparations of thiamine, riboflavin, niacin, pyridoxin and pantothenic acid

In order to supply vitamin B complex parenterally, recourse must be had to parenteral liver extract Heretofore, crude liver extracts — that is, extracts containing 1 or 2 units of antipernicious anemia factor per cubic centimeter — have been used for this purpose, in the belief that the concentration of the various other factors would be decreased in preparations containing 15 units of anti-pernicious anemia factor per cubic centimeter The fallacy of this belief is demonstrated in an extremely important paper by Clark,⁹⁵ who shows that concentrated liver extract (an average of four

preparations containing 15 units of anti-anemic factor per cubic centimeter) contains 19 times as much riboflavin, 11 times as much niacin, 11 times as much pantothenic acid and 22 times as much *L casei* factor as does an equal amount of crude liver extract (2 units per cubic centimeter) The concentration of thiamine in parenteral liver extract is minimal Furthermore, Clark shows how markedly the nutrition of the animals whose livers are used and the methods of preparation employed by different manufacturers affect the concentrations of the vitamin B components in the final product In one concentrated extract, for example, the riboflavin content was 205 microgm per cubic centimeter, whereas in a crude extract it was only 12 microgm Similarly, the concentration in micrograms per cubic centimeter ranged for niacin between 109 and 3161, for pantothenic acid between 5 and 1710, and for *L casei* factor between 02 and 872 Clark's figures do not include all the vitamin B fractions, but the sample suggests that the concentrations of other nutritional factors in parenteral liver extracts are subject to an equally great variation In view of these facts, it would be most advantageous if manufacturers analyzed some of their liver extracts for the known vitamin B fractions and printed the results on the label It is true that some preparations to which thiamine, riboflavin and niacin are added are labeled, but the figures on most of these preparations indicate the amounts of synthetic vitamins added and tell nothing of the vitamin B content of the liver extract itself

Obviously, no definite indications for parenteral vitamin B complex therapy can be given To certain patients, however, whose intake or absorption of the factors comprising the vitamin B complex has been impaired for more than four weeks, intramuscular injections of liver extract can be given with advantage Such patients include those with chronic ulcerative colitis or sprue and those who, after prolonged pyloric obstruction, are subjected to gastrectomy with complete, if temporary, elimination of food by mouth So far as one can judge clinically, the functional disorders that often follow gastrectomy⁹⁶ are at times greatly ameliorated after parenteral liver extract is given⁹⁷ The dosage, as can be deduced from Clark's figures, is anyone's choice Three to six cubic centimeters (always intramuscularly, never intravenously) weekly is used by many Since the available information suggests that the concentrations of the vitamin B components are not greatly different in the crude and concentrated extracts, the determining factor in choosing a liver extract for parenteral injection seems to be its cost On the other hand, crude extracts may contain essential substances that have not yet been identified

VITAMIN C

The concentration of vitamin C (ascorbic acid, cevitamic acid) in the human plasma ranges be-

average excretion in hospital patients.⁸² Again the results were similar, whether the nicotinamide was given orally or intravenously. Only 10 per cent of an intravenous dose of 5 mg per kilogram was recovered, chiefly as trigonelline, in the urine by Field and his associates.⁷² Ellinger and Benesch⁸³ testing for nicotinamide methochloride, obtained a 12 to 13 per cent recovery in twenty-four-hour urine collections after 100 mg of nicotinamide had been given orally or subcutaneously to normal subjects. On the other hand, Najjar⁷⁹ found that an oral dose of 100 mg of nicotinamide was followed by a urinary excretion of 2.1 to 4.0 mg of N-methyl nicotinamide in four hours, but that somewhat larger excretion figures were obtained with parenteral load tests. Similarly, an oral dose of 50 mg in children with nonhepatic disease was followed by a 3 to 7 per cent excretion in four hours, whereas the excretion ranged between 5 and 12 per cent after 20 mg had been given intravenously.⁷⁴

Although the urinary excretion of niacin after load tests with nicotinamide may be decreased in pellagrins and other patients with low niacin stores, it does not appear possible to saturate man with nicotinamide, as can be done with vitamin B₁ or riboflavin. The daily ingestion of large doses (50, 100 and 200 mg) of nicotinamide, for example, increases the urinary output of the vitamin but moderately⁷⁶ or not at all.^{78, 81} The reason for this is not clear. Either nicotinamide is stored or destroyed in the body no matter how much is given in excess of the body's needs, or all its derivatives appearing in the human urine have not yet been identified.

On the basis of what is known concerning niacin metabolism and excretion, it appears that less than 20 per cent, and often no more than 10 per cent, of a dose of nicotinamide is excreted in the urine. The figures are not affected by the size of the dose and are only slightly influenced by the route of administration. In deficient subjects, the urinary loss may be less, but it does not increase markedly in subjects who should theoretically be saturated.

Requirement. The National Research Council¹ recommends 18 mg of niacin daily for a moderately active male of 70 kg. This allowance is suspected of being far above the minimum needs,⁷⁷ but actually, knowledge of the human requirement for niacin is extremely scanty.⁸⁴ Obviously, the relatively unsatisfactory state of saturation tests with niacin or its amide contributes to the uncertainty that beclouds knowledge concerning man's niacin needs.

By analogy to other vitamins, it is assumed that the requirement for niacin is roughly parallel to one's total metabolism. Thus, 6 mg of niacin is recommended per 1000 calories for the normal person.¹ In illness, 10 mg of nicotinamide per 1000 calories may be suggested as an adequate dose for parenteral administration, although the influence of fever, starva-

tion and thyrotoxicosis on man's niacin requirement is totally unknown.⁸⁵ Man's capacity to store niacin or its derivatives is also an unexplored subject,⁷⁶ although studies in dogs (which, incidentally, can be saturated) suggest that a limited storage of the vitamin occurs.⁸⁶ By analogy with riboflavin, one may suggest that the daily parenteral dose of 10 mg per 1000 calories should be supplemented with 40 mg of nicotinamide if it appears that the patient has had a deficient intake or absorption of this vitamin for more than two weeks, or if he is being subjected to roentgen therapy.⁴⁶ The total daily dose would then be 60 to 70 mg of nicotinamide or about one third of the daily dose recommended by Spies⁴³ for the treatment of mild pellagra.

Certain diets seem to influence man's requirement for niacin,⁸⁴ but the effects of parenteral water, glucose, saline solution, amino acids and other vitamins are unknown. As is true of riboflavin, however, niacin storage in rats appears to be promoted when the animals are adequately supplied with protein.^{85, 86}

Biosynthesis of nicotinamide is not only said to occur in the human intestine, but it is also believed to contribute a substantial part of the nicotinamide requirement.⁸³ The administration of sulfonamides that act principally within the gut's lumen depresses this biosynthesis.⁸³ Whether the nicotinamide thus formed is available or nutritionally significant during periods of illness or complete starvation is unknown.

OTHER MEMBERS OF THE VITAMIN B COMPLEX

Many other water-soluble members of the vitamin B complex have been identified and studied. Two that have been synthesized and are commercially available for parenteral administration are pyridoxin (vitamin B₆) and pantothenic acid (often sold as its sodium or calcium salt). It has not been established unequivocally, however, that pyridoxin and pantothenic acid are essential for man, and the part, if any, played in human nutrition by these two factors has not been defined.

In man, the concentration of pantothenic acid has been reported as ranging from 19 to 32 microgm per 100 cc of whole blood in one series⁸⁸ and from 3 to 9 microgm in another.⁸⁷ Following the intravenous injection of 100 mg of either calcium or sodium pantothenate, a procedure that causes no reactions, blood levels and urinary excretion of pantothenic acid undergo a transient elevation.⁸⁸ In dogs, the following contrast in urinary excretion obtains after oral and intravenous administration of pantothenate.

DOSE mg/kg	TWO-HOUR EXCRETION
	%
1 (orally)	0
1 (intravenously)	25
4 (orally)	1-5
4 (intravenously)	41-57

The short period of urine collection may have influenced these results, but the peak in the excretion passed before the end of the two-hour period, even in the oral tests⁸⁹

A pantothenic acid intake of 10 or 11 mg per day has been estimated to be a safe level for man⁸ ⁹⁰ In adult dogs, large daily doses of calcium pantothenate (40 mg orally) seem to bring about enough storage of this substance so that the dogs can subsist for two or three months on a diet deficient in pantothenic acid⁹¹

Pyridoxin excretion in the urine contrasts with pantothenic acid in that the excretion of the former appears to be independent of the route of administration. An oral dose of 100 mg of pyridoxin in man is followed by a 75 per cent recovery in the urine four hours later⁹² After an intravenous dose of 50 mg, the urinary recovery in one hour lies between 8 and 9 per cent,⁹² ⁹³ a figure that is practically identical with the results of the oral test. In spite of the apparent ability of the body to "take up" injected pyridoxin, one should be cautious in concluding that the huge doses that have been recommended for certain disorders such as irradiation sickness or agranulocytosis are actually economical and rational from the viewpoint of the body's ability to utilize this substance. It should be recalled that the assay for pyridoxin and knowledge concerning its metabolism and that of related compounds leave considerable room for improvement⁸

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OTHER MEMBERS OF THE VITAMIN B COMPLEX

Many other water-soluble members of the vitamin B complex have been identified and studied. Two that have been synthesized and are commercially available for parenteral administration are pyridoxin (vitamin B₆) and pantothenic acid (often sold as its sodium or calcium salt). It has not been established unequivocally, however, that pyridoxin and pantothenic acid are essential for man, and the part, if any, played in human nutrition by these two factors has not been defined.

In man, the concentration of pantothenic acid has been reported as ranging from 19 to 32 microgm per 100 cc of whole blood in one series⁸⁶ and from 3 to 9 microgm in another.⁸⁷ Following the intravenous injection of 100 mg of either calcium or sodium pantothenate, a procedure that causes no reactions, blood levels and urinary excretion of pantothenic acid undergo a transient elevation.⁸⁸ In dogs, the following contrast in urinary excretion obtains after oral and intravenous administration of pantothenate.

DOSE mg/kg	TWO-HOUR EXCRETION
	%
1 (orally)	0
1 (intravenously)	25
4 (orally)	1-5
4 (intravenously)	41-57

No large stores of vitamin C can be laid down in the human body¹⁰ On the other hand, a saturated patient suffering from tuberculosis can stay on a vitamin C deficient diet for "several weeks" before his plasma level falls below 0.78 mg per 100 cc¹⁰¹ In the classic experiment of Crandon et al,¹²⁰ the plasma level fell below 0.8 mg per 100 cc almost immediately after a normal subject, previously on an average diet, started a diet poor in vitamin C In forty-one days, the level was zero Definite symptoms and signs of deficiency did not appear, however, until the subject had abstained from ascorbic acid-containing food for four months Thus, although it may take some time for severe tissue depletion of vitamin C to occur, it appears advisable to give vitamin C parenterally to any patient who is unable to take the vitamin by mouth or who is presumed to have had a deficient intake for a week or more

The plasma level of vitamin C as an index of a patient's ascorbic acid stores has had its supporters and its detractors For clinical purposes, however, it offers a fairly simple and not too inaccurate means of gauging a patient's status with respect to vitamin C^{98, 100, 111} Hence, if facilities are available for quantitating the plasma vitamin C content, much less guesswork must be used in estimating the needs of the depleted patient If such facilities are not available, one must again be guided by extremes A patient with frank scurvy has to ingest 700 mg of vitamin C daily for seven to ten days (total, about 5 to 6 gm) before he becomes saturated^{121, 122} For normal subjects who have depleted their stores by subsisting on a vitamin C-poor diet, 100 mg by mouth daily for a month saturates the tissues adequately¹¹⁸ When 1 gm is given daily by intravenous injection, a total of 4 to 6 gm is needed to resaturate a normal subject with experimental scurvy¹²⁰ In a patient with laboratory evidence of low vitamin C stores (low plasma level and low urinary excretion after a saturation test), a total of 1.5 to 2.8 gm appears necessary to achieve saturation⁹⁸ Consequently, if a patient requiring vitamin C by parenteral routes is believed to have deficient stores of this vitamin, either because of his dietary history or because of low plasma ascorbic acid levels, 500 mg daily for a week appears to be sufficient to build up his stores If there is great urgency, 1 to 2 gm can apparently be given intravenously with satisfactory results⁹⁸

VITAMIN A

The parenteral injection of the fat-soluble vitamins, of which vitamin A is one, presents special problems unless water-soluble preparations are available The intravenous administration of finely emulsified fats is possible, but the preparation and preservation of such emulsions are not easy, and none are sold for general use The intramuscular route is, of course, frequently used, but, as is evident

if one follows the fate of radio-opaque oil that has been given intramuscularly, months may pass before most of the material is mobilized from the site of injection¹²³ Obviously, any fatty vitamin administered intramuscularly cannot be expected to provide the recipient with a large dose that is immediately available for the body's needs

When measured with the technic commonly used in clinical studies, the plasma level of vitamin A normally lies between 30 and 80 microgm (100 to 250 *U S P* units) per 100 cc^{124, 125} The carotene (provitamin A) concentration is usually 40 to 200 microgm per 100 cc of plasma^{5, 124} With microtechnics, somewhat lower vitamin A levels are obtained¹²⁶

When large doses (75,000–100,000 units) of vitamin A are injected intramuscularly in man, the plasma level of the vitamin is not elevated^{127, 128} Even in sprue and celiac disease, disorders characterized by a severely impaired intestinal absorption of fat-soluble vitamins, massive oral doses may produce a small rise in the vitamin A level of the plasma,^{129, 130} but the same doses intramuscularly are without such an effect¹²⁹ This fact does not necessarily mean that intramuscular administrations are ineffective In patients with obstructive jaundice, the livers of those who have been treated with intramuscular vitamin A contain on the average more of this vitamin than do the livers of untreated patients¹²⁸ Judged on the basis of growth effects and hepatic storage, animals use vitamin A equally well, whether given orally or parenterally^{131, 132} The literature on this point, however, does not report uniform results, others stating that vitamin A given intramuscularly to rats is only 10 to 15 per cent as effective as the same amount given orally¹³³ It seems reasonable to conclude as follows: the oral route is incomparably better than the intramuscular for the administration of vitamin A Parenterally injected vitamin A is probably available for utilization, but the rate of its liberation from the injection site is so slow and the rate of metabolism or storage is so rapid that the plasma level is not materially changed The urinary excretion of vitamin A is not significant

Vitamin A in propylene glycol is well utilized by rats after intramuscular injection,¹³⁴ but 70,000 units of the same preparation does not elevate the plasma level in human subjects and produces considerable pain at the injection site⁹⁷ The utilization of carotene after parenteral injection is even less efficient than that of vitamin A¹³¹

Unlike the water-soluble vitamins, vitamin A can be stored in large quantities in such depots as the human liver Twelve million, five hundred thousand units given by mouth over the course of five days can raise the average hepatic concentration of vitamin A from 100 to 366 microgm per gram of fresh liver tissue.¹³⁴ Once well fortified with oral doses of vitamin A, normal subjects can subsist for

tween 0.3 and 1.8 mg per 100 cc, levels of 0.8 mg or over occur in those whose intake of vitamin C is ample.⁹⁸⁻¹⁰⁰ Whole blood concentrations average 0.1 to 0.2 mg per 100 cc higher,⁹⁸ chiefly because of the high vitamin C content of white cells (25 to 38 mg per 100 cc⁹⁹). In red cells, the level is 0.4 to 1.5 mg per 100 cc.⁹⁹

Ascorbic acid is water soluble and is suitable for parenteral injection, preferably as sodium ascorbate. Following intravenous injection, the plasma level rises markedly, but within a few hours most of the excess vitamin is removed from the plasma.¹⁰¹ Unlike thiamine or riboflavin, vitamin C appears to have a renal threshold that varies from person to person but usually lies between 1.1 and 1.8 mg per 100 cc of plasma.^{101, 102} Once its plasma level is in excess of the threshold, ascorbic acid is excreted in the urine, the rate of excretion depending on the plasma level, the rate of glomerular filtration and the maximal rate of tubular reabsorption.¹⁰³ Thus, if the plasma vitamin C level is 5 mg per 100 cc, the glomerular filtration rate 120 cc per minute, and the maximum rate of tubular reabsorption 2.16 mg per minute,¹⁰³ about 4 mg of the vitamin is excreted in the urine per minute. The rate of urine flow does not affect the amount of vitamin excreted.¹⁰³ In man, the maximal rate of tubular reabsorption of vitamins is not impaired by infusing glucose solutions, even when the plasma glucose level is raised above 300 mg per 100 cc.¹⁰³ In dogs, on the other hand, simultaneous intravenous administration of glucose and ascorbic acid is said to decrease the tubular reabsorption of ascorbic acid and thus lead to an increased excretion of the vitamin.¹⁰⁴

Since the intravenous injection of a saturation-test dose of vitamin C is much likelier to elevate the plasma level than an oral dose of the same size, a definite difference in urinary excretion of vitamin C is expected between the two methods of administration. On the whole, this tends to be the case. In deficient patients, the urinary excretion of ascorbic acid five hours after 400 mg had been given orally totaled only 2 to 5 mg, after the intravenous injection of the same dose, it amounted to 30 to 80 mg.¹⁰⁵ In another series, unsaturated subjects excreted less than 20 per cent of a 100 or 200 mg test dose in 24 hours, whether it was given orally or intravenously.¹⁰⁶ Saturated subjects, however, excreted 60 to 100 per cent, with the loss slightly larger after intravenous injection. Faulkner and Taylor¹⁰¹ found a more marked difference, their deficient subjects excreted only 20 mg in twenty-four hours after 1 gm of vitamin C had been given orally, whereas they excreted 296 mg after an intravenous test dose. Normal subjects reported in their study excreted 200 mg after taking 1 gm by mouth and 403 mg after receiving this dose by vein. When 200 mg was given intravenously to apparently normal soldiers, an average of roughly 15 per cent (range, 5 to 103 mg) was recovered in the urine six

hours later.¹⁰⁷ In a deficient subject, 1.5 gm of vitamin C given orally was followed by an 82-mg loss in the urine within twenty-four hours, whereas the loss in a comparable subject after the same dose had been given by vein was 582 mg.⁹⁸ On the other hand, a deficient subject excreted only 134 mg after an intravenous administration of 1.5 gm. It is thus apparent that intravenous injection of vitamin C leads to spillage in the urine.^{108, 109}

On the other hand, the avidity of the tissues for ascorbic acid plays a major role. Vitamin C is apparently removed so rapidly from the plasma of a deficient subject that the plasma level soon drops below the renal threshold, even after intravenous injection of the vitamin. So far as the parenteral ascorbic acid therapy of patients is concerned, the urinary loss after rapid intravenous infusion in moderately depleted subjects averages about 20 per cent, in normal subjects about 40 per cent, and in saturated subjects over 80 per cent.¹¹⁰ A slow infusion of vitamin C diluted in saline solution presumably entails less of a loss, especially if the amount of ascorbic acid given per minute is extremely small and if the recipient's need for the vitamin is great.

Requirement The adult man of 70 kilograms is thought to need 75 mg of ascorbic acid a day, and a lactating woman 150 mg.¹ As holds true for other vitamins, these allowances are thought by some to be safe rather than minimum.^{100, 111, 112} When fever is present, the metabolism of vitamin C may be altered.^{35, 113} Plasma ascorbic acid, for example, is lowered during the course of an infectious fever but not during an artificial fever induced by mechanical means.¹¹⁴ Another author believes fever may lead to the destruction of 100 mg or more of ascorbic acid daily,¹¹⁵ but the evidence for this is not clear cut.³⁵ Leukemia, or its treatment, is said to destroy vitamin C in the body,⁹⁸ and the requirement for the vitamin may be increased in hyperthyroidism.³⁸ When saturation tests are used, a patient with an infection may excrete no more ascorbic acid than a scorbutic subject.¹⁰¹ According to Harris and his co-workers,^{116, 117} the requirement for vitamin C is increased in osteomyelitis, Addison's disease and systemic infections. Although ascorbic acid is excreted in sweat, the amount thus lost is minimal.³⁵ Finally, various drugs and high altitudes may affect the metabolism of vitamin C.¹¹⁸ In view of the high allowance recommended for a lactating woman, and the scattered suggestions that ascorbic acid consumption is increased in febrile illnesses, a 200-mg dose of vitamin C may be suggested as a daily maintenance dose for the patient who requires parenteral administration of the vitamin. A 25 per cent loss in the urine would still leave 150 mg for the patient's needs. It should be noted that this dose is considerably less than the 500 mg per day recommended by Wolfer and Hoebel,¹¹⁹ but exceeds the 50 mg advocated by Spies.⁴³

however, been synthesized tetra-sodium 2-methyl-1-4-naphthohydroquinone diphosphoric acid ester (Synkayvite), 2-methyl-1-4-naphthohydroquinone-sodium bisulfite (Hykinone) and 4-amino-2-methyl-1-naphthol hydrochloride (Synkamin)

The water-soluble nature of these compounds makes them suitable for intravenous use and preferable to menadione for intramuscular use when, as is often the case, immediate availability of the vitamin is desired.¹⁵³ On the other hand, the use of these compounds from the viewpoint of dosage is unsatisfactory, since the manufacturers merely give the total weight of the menadione derivative on the label and do not indicate its vitamin K activity in terms of simple menadione. When an ampule contains 4 mg of Hykinone, for example, only 2.5 mg of material with vitamin K activity is actually present.¹⁵⁴ The same holds true for Synkayvite, but here the situation is further complicated by the fact that this substance, although only half as potent as menadione on a weight-for-weight basis, is said to be one and a half times as effective when the substances are compared molecule for molecule.¹⁵⁵⁻¹⁵⁷ Thus, when a certain weight of these water-soluble compounds is injected, only a part — roughly 50 to 70 per cent — of the dose can be considered to have vitamin K activity.

The nature of a substance with vitamin K activity and the route of its administration determine to some extent the rapidity of its action and the duration of its effect. When colloidal vitamin K₁, a naturally occurring compound, is given intravenously to patients with obstructive jaundice, a rapid increase in prothrombin concentration occurs within four hours, and normal prothrombin times are maintained for about two days after a 0.4-mg dose, and for ten to twenty-five days after a 10-mg dose.^{158, 159} Similarly, 10 mg of colloidal menadione intravenously effects normal prothrombin levels for ten days.¹⁵³ In these instances, a fatty vitamin is rapidly made available to the liver but no obvious loss of the vitamin occurs. When water-soluble preparations are given intravenously, however, the beneficial effect may be less pronounced, and only of short duration.¹⁵³ A similar result is reported by Kark and Souter,^{159, 160} who found that intravenous injections of a water-soluble derivative of menadione (the bisulfite complex) increased the concentration of prothrombin for only one or two days, whether the amount injected was the equivalent of 1 or 6 mg of menadione. An intramuscular dose of the same bisulfite complex, equivalent to 2 mg of menadione, was effective, however, for several days. It has therefore been suggested that water-soluble substances with vitamin K activity, when given intravenously, offer a rapid but temporary supply of vitamin K to the liver, the transient character of the effect being ascribed to urinary excretion or destruction of the vitamin.^{153, 159, 160} Except when the circulation is impaired, intramuscular injection

of the water-soluble vitamin K preparations reduces the prothrombin time practically as quickly as the intravenous, but presumably less loss occurs since the whole dose is not delivered to the blood stream instantaneously. For long-term therapy the intramuscular use of menadione itself (in oil) is perfectly satisfactory.

In 1940, Dam¹⁶¹ stated that 5 to 10 mg of menadione daily is "entirely sufficient" for an adult person. Clinical studies suggest that this dose amply provides for the needs of patients. Two milligrams of menadione given to jaundiced and hypoprothrombinemic patients has, in the absence of liver disease, restored prothrombin levels to normal for almost a week,¹⁶² and in one case with an absorption defect the same dose apparently sufficed for a whole month.¹⁶³ According to studies already quoted, 1 mg of vitamin K₁ per day is sufficient to prevent hypoprothrombinemia.^{153, 163} Ten milligrams of a water-soluble vitamin K analogue given subcutaneously maintained normal prothrombin times for two to three days in patients with evidence of vitamin K deficiency.¹⁶⁴ Andrus and Lord¹⁶⁵ recommend 2 mg of menadione every three to ten days. In infants, 10 mg of menadione prevented a fall in the blood's prothrombin concentration for at least twenty-six to twenty-eight days,¹⁶⁶ and 1.25 mg of a water-soluble preparation was effective in reducing a prolonged prothrombin time to normal and maintaining it in this range.¹⁶⁷ It has also been concluded that a daily dose of 0.5 to 2 microgm of water-soluble vitamin K analogues is sufficient to prevent hemorrhagic disease in newborn infants.^{167, 168} The daily requirement for an adult on this basis would be about 0.1 mg per day.¹⁶⁹

In bile-fistula dogs, one to three months may pass before prothrombin levels begin to fall.¹⁷⁰ Nevertheless, storage of vitamin K, when compared with the storage of the other fat-soluble vitamins, is limited. Because large doses (over 20 mg daily) of the naphthoquinones may produce a mild hemolytic anemia,¹⁷¹ extensive studies in man on the storage of vitamin K are not easily feasible. Nevertheless, there is evidence that increasing dosage does not lead to increasing storage, but rather to increasing wastage.¹⁶⁸

One may conclude that for rapid and effective treatment with vitamin K, the intramuscular injection of the water-soluble preparations is advisable, with the admonition that the injected amount has only 50 to 70 per cent of the vitamin K activity of a similar amount of menadione. If the intramuscular route is employed, 4 mg of the water-soluble substance every two to three days is probably effective. If the vitamin is given intravenously, 2 mg daily is suggested as a dose.

In the treatment of hypoprothrombinemia, however, one cannot rely on theoretical requirements, one must be guided from time to time by actual determination of the prothrombin level. Since these

six months on a diet deficient in this vitamin without decreasing their plasma level of vitamin A ¹³⁵

The daily requirement of vitamin A for the adult has been set at 5000 units. Whether there is an increased requirement for vitamin A, or rapid depletion of its stores, in disease is difficult to tell. An almost endless list of diseases, it is true, may be associated with a decrease in the plasma level of vitamin A, but this level is too dependent on other factors, such as hepatic function, to serve as a good index of the body's stores. As Popper and his associates ¹³⁴ have said, a high plasma level often suggests high or normal liver stores, but the reverse does not hold true.

In view of the body's ability to store vitamin A and the rather unsatisfactory results obtained from its intramuscular use, sound indications for injecting vitamin A parenterally occur but rarely. Conceivably, patients with a long-standing exclusion of bile from the gut, or with steatorrhea from other causes, may benefit from such injections, but even in these cases, large oral doses — that is, about 250,000 units daily — probably increase body stores more efficiently. Whenever possible it seems reasonable to build up a patient's vitamin A reserves by means of several large oral doses before any operation is undertaken that might interfere with food ingestion or absorption for a protracted period of time.

VITAMIN D

Vitamin D, a fat-soluble vitamin, appears in plasma in concentrations ranging from 66 to 165 *U S P* units per 100 cc ¹³⁶. After oral administration of huge doses (50,000 to 500,000 units), the plasma concentration of vitamin D may temporarily approach that of cod-liver oil ¹³⁶. Following the administration of such large amounts, considerable storage of the vitamin presumably occurs, since three to six months elapse before the vitamin D content of the plasma returns to normal ¹³⁶. Corroborative evidence of the body's capacity to store vitamin D is obtained from the facts that a single large dose of calciferol (vitamin D₂, irradiated ergosterol) protects infants against rickets for eight to twelve weeks ¹³⁷ and provides puppies with adequate growth for one year ¹³⁸. A peculiar feature of this storage is that tissue analysis for vitamin D fails to reveal any capacious storage organ for the vitamin ¹³⁸.

Vitamin D is apparently utilized when given by the intramuscular route, for protection against rickets has been achieved in infants by giving 600,000 units of either vitamin D₂ or D₃ (activated 7-dehydro-cholesterol) parenterally ^{133 139 140}. If the oily solution containing the vitamin D₂ is diluted by ether, it is said that the absorption from the intramuscular injection site is more rapid, and that rachitic phenomena regress as promptly as after oral therapy ¹²³. In other studies, the parenteral in-

jection of vitamin D₂ was much less effective than injected vitamin D₃ in treating infantile rickets ¹⁴¹. In chickens, the utilization of vitamin D appears to be enhanced if vitamin D in propylene glycol is used for parenteral injections ¹⁴².

One may therefore conclude that vitamin D injected intramuscularly is in large part available for metabolic uses. On the other hand, the requirement of the adult for this vitamin is uncertain, ¹ and it appears that storage is adequate to provide for fairly long periods of depletion. Hence it is doubtful that parenteral injections of vitamin D have to be used in maintaining the nutrition of a patient who is unable to take this vitamin orally.

VITAMIN E

The serum tocopherol (vitamin E) level, as determined by chemical methods, ranges between 0.60 and 1.60 mg per 100 cc, ^{143 144} but lower levels, averaging 0.20 mg per 100 cc, have also been reported ¹⁴⁵. Oral administration of vitamin E elevates the serum tocopherol level, ¹⁴⁴ but as in the case of vitamin A, intramuscular injections (100 mg of alpha-tocopherol) do not ¹⁴⁴. In rabbits, the intramuscular injection of oil-soluble tocopherols ¹⁵ is also ineffective in curing the signs of deficiency, ¹⁴⁶ but a water-soluble preparation is said to be curative when given parenterally ¹⁴⁷.

Storage of vitamin E occurs in the liver ^{148, 149} and in the abdominal fat ¹⁵⁰ of the rat. In human livers, a somewhat similar storage may take place ¹⁴⁸. Vitamin E is not excreted in the urine ¹⁴⁹.

Vitamin E has been administered to patients for a great variety of illnesses, chiefly those of the neuromuscular system, but the effects of tocopherol deficiency in man are undefined. For this reason, the significance of vitamin E in human nutrition is uncertain, and daily allowances that have been suggested on the basis of interesting but indirect evidence ¹⁵¹ must await further study before they can be accepted.

VITAMIN K

Naturally occurring vitamin K is a fat-soluble substance that appears to be utilized by the liver in making prothrombin. At present, the vitamin K content of the blood cannot be measured directly, but the blood's prothrombin concentration provides a good index of the availability of vitamin K to the body, provided the patient does not suffer from hepatic disease and has not been treated with dicumarol ¹⁵².

The situation with respect to vitamin K is rather unusual in that the naturally occurring substances with vitamin K activity have been supplanted by an equally active synthetic product, menadione (2-methyl-1, 4-naphthoquinone). This material is fat-soluble and suitable for intramuscular injection. A related series of water-soluble compounds has,

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levels are known to drop acutely after operations,¹⁶⁵⁻¹⁷² a dose of vitamin K equivalent to 4 mg of menadione may be given daily in the immediate preoperative period. Large doses of vitamin K may also be tried in combating the hypoprothrombinemia of hepatic disease¹⁷¹ or that following the exhibition of dicumarol.¹⁶⁴

Biosynthesis of vitamin K occurs actively in the human intestine and may provide a considerable proportion of man's requirements for this vitamin. When sulfonamides, such as sulfaguanidine or succinylsulfathiazole, are used, the biosynthesis of vitamin K drops off sharply.^{51, 173} This fact is of practical importance in the treatment of such disorders as ulcerative colitis in which a poor diet, diarrhea and the exhibition of intestinal disinfectants may combine to bring about a vitamin K deficiency.

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last examiner, since the mass does not seem to fit any obvious diagnosis

It would be nice to explain all the symptoms on the basis of one disease, and the one disease that might explain them is syphilis. I have already mentioned the possibility of cerebrovascular syphilis and latent neurosyphilis. The vascular accident could then be due either to syphilitic endarteritis or to rupture of a small aneurysm on a syphilitic basis. Syphilitic endarteritis is much likelier. Can we explain the kidney damage and the resulting uremia on the basis of syphilis? This was obviously not a case of syphilitic nephrosis. It could have been a late type of vascular nephritis, such as one finds in syphilis and which is difficult to differentiate from ordinary vascular nephritis. It may terminate in uremia, like any other nephritis. One might consider the mass in the abdomen as due to an abdominal aneurysm—a thrombosed abdominal aneurysm on a syphilitic basis. Unfortunately we have no data to confirm it, and I am not inclined to accept it.

The mass might have been due to a malignant tumor, such as a tumor of the stomach, gall bladder or pancreas. One might then consider metastasis to the brain and other organs, such as the kidneys. Obviously metastases alone would not cause acute hemiplegia of the sort described. On the other hand, hemorrhage into the appropriate metastasis might give a picture similar to that of this patient. This is only surmise; we do not have enough evidence for it.

Another surmise, also farfetched, is a dissecting aneurysm. The dissection could have worked its way up to occlude the right carotid artery and its way down to the abdominal aorta, where a mass resulting from weakening of the wall of the aorta might have been felt. We have no confirmatory evidence, however, such as occlusion of the great vessels of the leg or the presence of excruciating pain at the onset.

Let us disregard syphilis for the time being and consider a disease that might cause this type of cerebrovascular accident, namely, generalized arteriosclerosis with hypertension. This would certainly explain the hemiplegia. The uremia might have resulted from the effects of a generalized infection on previously damaged kidneys, the previous damage having been on a vascular basis.

I wonder if the x-ray films will help so far as diagnosis is concerned.

DR MILFORD D SCHULZ. The only thing that is at variance with what is described in the protocol is that the pulmonary lesion is in the right middle lobe rather than in the right upper lobe. Whether it is due to consolidation or to bronchial obstruction I do not know. There is a lot of calcification in the wall of the aorta, and it goes all the way down to the diaphragm. But the aorta itself can be fairly well traced.

DR LERMAN. Do you see the mass?

DR SCHULZ. I see no abdominal mass. It could easily be missed, however, because the film is underexposed and a mass would be difficult to differentiate from the liver and kidney.

DR LERMAN. The pain might have been due to syphilis if we assume that this man had a tabetic crisis, but since there is no evidence of active tabes, we cannot ascribe the pain to it. I am not able to explain the pain, other than on the possibility of its association with kidney damage. Abdominal pain is sometimes seen in impending uremia.

My diagnoses are as follows: arteriosclerotic and hypertensive heart disease, syphilis, including latent neurosyphilis and cerebrovascular syphilis, cerebrovascular thrombosis, probably due to syphilis but possibly to simple arteriosclerosis, terminal pneumonia, vascular nephritis on an arteriosclerotic basis, uremia, and possibly abdominal aneurysm.

DR JOST MICHELSEN. Where was the vascular process in the brain located?

DR LERMAN. I do not know the exact location.

DR MICHELSEN. Do you think that the cerebral symptoms can be explained by one lesion or do you assume that the patient had several lesions?

DR LERMAN. He had a left hemiplegia, with left facial weakness.

DR MICHELSEN. How do you explain the difficulty with speech?

DR LERMAN. The patient had a hemiplegia and difficulty in speech without aphasia, which imply motor difficulty.

DR MICHELSEN. What was the motor difficulty? The patient had a mild facial weakness. We are not told what the defect was. How do you then explain the speech difficulty?

DR LERMAN. I do not believe that I can, other than on basis of motor weakness.

DR MICHELSEN. What I am driving at is that it is likely that he had more than one lesion. Could he have had multiple emboli? Could he have had auricular fibrillation before he was admitted to the hospital?

DR LERMAN. Without any previous evidence of auricular fibrillation or anything suggestive of it on admission, one can only make a guess. It is not infrequent for a man of this age to develop auricular fibrillation as a terminal event, with a resulting fall in blood pressure. Such a picture is often seen in patients with ordinary arteriosclerotic heart disease. I see your point, namely, that he might have had several emboli going to different parts of the brain, or several thromboses. I assume, however, that the speech difficulty was purely a temporary motor affair, due to muscle weakness and inco-ordination rather than to aphasia. I have seen it before in patients with a left hemiplegia.

DR MICHELSEN. But one usually finds some evidence for it on examination. The evidence here for such a situation is scanty.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor**

BENJAMIN CASTLEMAN, M D, *Acting Editor*

EDITH E PARRIS, *Assistant Editor*

CASE 31401

PRESENTATION OF CASE

A sixty-eight-year-old man was admitted to the hospital because of inability to speak coherently. The history was obtained from relatives.

Five days before admission, after an evening of normal, quiet conversation, he suddenly asked in a thick, almost incoherent voice to be taken to bed. Since that time he had slept almost constantly and had eaten no food other than liquids. His bowels moved three days before admission. He urinated daily. Two days before the onset of this episode he had experienced nausea and some regurgitation and had vomited several times.

The patient was incoherent, incontinent and uncooperative. He seemed to be suffering from abdominal pain. Examination of the heart and lungs was negative. The abdominal muscles were tense. The liver and spleen were not palpable. A 5-cm nontender, nonpulsating mass was present in the epigastrium just to the right of the midline. The patient was not aphasic. The left arm and leg were weak, without spasticity. The optic disks were well outlined. There was questionable weakness of the left facial muscles. The tendon reflexes were active. The patellar reflexes were more marked on the left than on the right. Plantar flexion occurred on the right, but the response on the left was equivocal.

The temperature was 99.2°F, the pulse 80, the respirations 25, and the blood pressure 170 systolic, 90 diastolic.

Examination of the blood revealed a red-cell count of 3,400,000, with 12 gm of hemoglobin, and a white-cell count of 14,400, with 68 per cent neutrophils. The urine was normal. The blood Wassermann reaction was positive. A lumbar puncture five days after admission revealed clear fluid under an initial pressure equivalent to 105 mm of water, after withdrawal of 6 cc the pressure dropped to 78 mm. The respiratory fluctuations of pressure were normal. The fluid contained no white cells and 50 red cells per cubic millimeter. The total protein was 29 mg per 100 cc, and the gold-sol curve was normal. The spinal-fluid Wassermann reaction was negative.

*On leave of absence

A plain x-ray film of the abdomen showed no definite soft-tissue masses. There was extensive arteriosclerosis of the pelvic arteries.

On the twelfth hospital day the blood pressure fell to 125 systolic, 70 diastolic, and auricular fibrillation appeared. An electrocardiogram showed a PR interval of 0.17 second. The QRS complexes in Leads 1, 2 and 3 were upright, T_1 was flat, T_2 upright, and T_3 inverted. The T waves in Leads CF_1 and CF_4 were upright, the S wave in Lead CF_4 was normal. The serum nonprotein nitrogen was 188 mg per 100 cc, the white-cell count 6400, and the carbon dioxide 10 milliequiv per liter.

The temperature suddenly rose from a subnormal level to 101°F, and the respirations became rapid. Rales appeared in the right upper lobe, and x-ray films showed consolidation in that area. He expired a few hours later.

DIFFERENTIAL DIAGNOSIS

DR JACOB LERMAN: There are two points that I should like to question. Was the tumor mass in the abdomen felt by more than one observer? There is the note that it was felt on physical examination, but x-ray examination did not show a soft-tissue mass. Also, there was one negative urine examination. A little later the man went into uremia. Was there more than one urine examination, and if so, what did it show?

DR RONALD C SNIFFEN: There were two urine examinations, both were the same, with the exception that 5 to 8 white cells per high-power field were seen in the sediment on the second occasion. The specific gravity was 1.012.

DR LERMAN: We know that this man had certain pathologic conditions, which are described for us in the record. He had an acute onset of symptoms initiating the development of a cerebrovascular accident, due either to thrombosis or to hemorrhage. The absence of coma and the presence of premonitory symptoms two days previously make one think it was thrombosis rather than hemorrhage. The resulting left hemiplegia confirms the presence of the cerebrovascular accident. We know that he had syphilis, and he probably had latent neurosyphilis. He may also have had cerebrovascular syphilis. Then we also know that he developed an acute infection, — a terminal infection, — which probably precipitated the auricular fibrillation, drop in blood pressure and uremia.

The two points that are hard for me to explain are the abdominal pain, — although this was only surmise on the part of the examiner, inasmuch as the patient actually complained of nothing, — and the mass in the abdomen.

DR SNIFFEN: At least four people examined the patient. One was sure about the mass, two were vague, and the fourth did not feel it.

DR LERMAN: I prefer to take the opinion of the

on the left, on the right there was a small egg-sized tender mass. The posterior cul-de-sac was free, but there was some induration in the right vault.

The temperature, pulse, respirations and blood pressure were normal.

Examination of the blood showed a white-cell count of 7400 and a hemoglobin of 12 gm. The urine was normal.

On the fifth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. FREDERICK A. SIMMONS: In spite of the fact that the fallopian tubes are said to have been blocked, it is necessary to mention that any thirty-eight-year-old woman with abdominal pain and abnormal vaginal bleeding must be considered as a candidate for an ectopic pregnancy, especially when a mass is felt. Certainly the attack eleven days before admission, which consisted of a dark bloody discharge with severe, cramplike, suprapubic pain, a bearing-down sensation and tenderness, raises that possibility. The facts that she had previously had a twenty-eight-day menstrual cycle and that she was twelve days overdue make ectopic gestation a likely diagnosis. The record does not say how many years she had been married, but it does report that several years previously a lipiodol examination had shown that tubes were blocked.

I have seen several cases in which lipiodol suggested that the tubes were blocked but in which an immediate pregnancy occurred following this test. It is important to emphasize that the interpretation of lipiodol studies for patency of the fallopian tubes is extremely unreliable and that, although it is a necessary procedure in sterility investigation, one should not place too much reliance on the comment that the tubes are blocked, unless, of course, the oil fails to pass the uterine ends of the tubes. It would be helpful to be able to see these films.

The uterus is described as being three or four times its normal size, being movable and irregular, with an attached tender mass on the left. The literature reveals cases in which a uterine pregnancy occurred simultaneously with an ectopic pregnancy, but when pelvic masses are found on both the left and right sides, in addition to an enlarged uterus, the possibility of multiple fibroids presents itself. Since the temperature, pulse, respirations, blood pressure, white-cell count and urine were normal, we are probably not dealing with an inflammatory process, such as pelvic inflammation, a twisted ovarian cyst, tuberculosis of the uterus or adnexa or diverticulitis of the colon. I mention the latter because last winter we had a patient on the Gynecological Service who had vaginal bleeding and a tender mass and was thought to have had cancer of the cervix. Multiple biopsies were negative, and subsequent exploration revealed a ruptured divertic-

ulitis, with a pelvis as "frozen" as that usually seen in chronic pelvic inflammatory disease.

With the abnormal vaginal bleeding, cancer must also be mentioned, and in a woman of thirty-eight, carcinoma of the cervix or ovary is likelier than that of the fundus. Although cancer cannot be ruled out, the sudden onset of the symptoms is somewhat against the diagnosis.

A few months ago, while discussing a similar case in one of these conferences, I purposely avoided an obvious fact, namely, a past history of tuberculosis, which is what the pelvic disease turned out to be. Perhaps this patient's irregular bleeding, sterility, abdominal pain and masses were on the basis of an acid-fast infection, but I doubt it.

Presumably the possibility of pregnancy occurred to the house staff. You will note that operation was not performed until the fifth hospital day, and I suspect that an Aschheim-Zondek test was performed. At any rate the patient did come to an exploratory laparotomy. I am going to assume that the statement that the fallopian tubes were blocked is correct and to say that I do not believe that this woman was pregnant.

I believe that the likeliest diagnosis in this case is multiple fibroids of the uterus, with ovarian cysts, which are usually found with multiple fibroids. It would not be surprising, however, to find that she had an exacerbation of long-standing bilateral pelvic inflammation, since abnormal bleeding does occur in such cases.

CLINICAL DIAGNOSES

Fibroids of uterus
Tubal pregnancy?

DR. SIMMONS'S DIAGNOSES

Multiple fibroids of uterus
Simple cysts of ovaries

ANATOMICAL DIAGNOSES

Tubal pregnancy
Multiple leiomyomas of uterus
Chronic salpingitis

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Apparently an Aschheim-Zondek test was not performed, at least there is no note in the record to that effect.

At operation a hemorrhagic mass was found in the outer end of the right salpinx, which proved to be an ectopic pregnancy. The fimbriated ends of both tubes were destroyed and scarred — a finding that is consistent with an old inactive inflammatory process. The uterus contained multiple fibroids, the largest, which measured 9 by 5 by 5 cm., being subserosal and placed anteriorly on the right. The intramural fibroids varied from 1 to 3 cm. in diameter. A subtotal hysterectomy and right salpingo-oophorectomy were performed.

I should also like to ask about the occurrence of cerebral aneurysm on a syphilitic basis. Dr. Sniffen, how many cases of cerebral aneurysm have we seen in which syphilitic etiology was definitely established?

DR. SNIFFEN: It is extremely rare.

DR. LERMAN: I agree, I just put it down as a possibility. Vascular thrombosis on the basis of syphilis is much more frequent.

CLINICAL DIAGNOSIS

Cerebral thrombosis

DR. LERMAN'S DIAGNOSES

Arteriosclerotic and hypertensive heart disease
Syphilis, including latent neurosyphilis and cerebrovascular syphilis
Cerebrovascular thrombosis (right), due either to syphilis or to arteriosclerosis
Terminal pneumonia
Vascular nephritis, arteriosclerotic
Uremia
Abdominal aneurysm?

ANATOMICAL DIAGNOSES

Cerebral infarct, right internal capsule and corpus striatum
Carcinoma of stomach, with extension to omentum and metastases to liver and mediastinal and retroperitoneal lymph nodes
Hydronephrosis, hydronephrosis and mild chronic pyelonephritis, bilateral
Bronchopneumonia

PATHOLOGICAL DISCUSSION

DR. SNIFFEN: At the time of his death the patient was extremely emaciated.

The brain contained a 1.5-cm. infarct situated in the anterior limb of the right internal capsule and adjacent corpus striatum. Microscopically, the infarct seemed to be of approximately three weeks' duration.

The stomach contained a carcinoma involving the greater curvature and the neighboring anterior and posterior walls. The tumor extended from the pylorus to a point about 13 cm. proximal. The gastric wall was 3 cm. in thickness, but the mucosa was intact and there was no mass in the lumen, merely a diffuse infiltration that had not led to obstruction. The lymph nodes along the greater curvature were invaded, and the omentum and transverse colon were caught up in a firm mass of infiltrated fat, which was probably the mass felt on physical examination. Metastases were present in the liver and retroperitoneal and mediastinal lymph nodes. Tumor masses were found in the pelvis, and these surrounded and compressed the ureters, leading to hydronephrosis, hydronephrosis and a mild pyelonephritis.

Microscopically the tumor showed a peculiar combination of adenocarcinoma and scirrhous carcinoma; with signet-ring cells, it included islands of squamous epithelium. Consequently, I imagine that it can be called an adenoacanthoma.

In addition the patient had a severe bronchopneumonia.

DR. MICHELSEN: What caused the infarct?

DR. SNIFFEN: We found no syphilitic lesion in any part of the body. We saw no tumor cells within the vessels. One large vessel was thrombosed. It was our assumption, therefore, that the infarct was caused by arterial thrombosis.

CASE 31402

PRESENTATION OF CASE

A thirty-eight-year-old married woman was admitted to the hospital because of abdominal pain and abnormal vaginal bleeding.

Eleven days before admission the patient noticed a profuse dark bloody vaginal discharge, which was associated with a sharp stabbing, intermittent pain in the midline just above the pubis that was accompanied by tenderness and a bearing down sensation. These cramps were affected by change in position. She had noticed the usual engorgement and tenderness of the breasts that she associated with menstruation. The following day the discharge had a more normal color. Within five days the pain had become less severe, but it recurred after a pelvic examination.

Forty days before the onset of this discharge she had had her last normal menstrual period. She had always had a regular twenty-eight-day menstrual cycle. She normally had a profuse discharge for three days, which then became scanty for two more days. About two years previously, at the expected menstrual time, she had had bearing down cramps and had passed a single large clot followed by a fairly prolonged discharge, which stopped after ergot had been given. Her physician told her that she had had a spontaneous abortion. Except for this questionable episode, she had never been pregnant, and several years previously lipiodol insufflation was said to have shown that both tubes were blocked. She had had an appendectomy years before.

Physical examination revealed a well nourished and well developed young woman. The heart and lungs were normal. There was a firm tender mass about 5 cm. in diameter in the midline immediately above the pubis. To the right of this was an area of maximal tenderness and slight spasm of the abdominal muscles. A rectal examination was negative. A pelvic examination revealed a firm cervix. The fundus of the uterus appeared to be three or four times its normal size. The uterus was freely movable and irregular, with an attached tender mass.

on the left, on the right there was a small egg-sized tender mass. The posterior cul-de-sac was free, but there was some induration in the right vault.

The temperature, pulse, respirations and blood pressure were normal.

Examination of the blood showed a white-cell count of 7400 and a hemoglobin of 12 gm. The urine was normal.

On the fifth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

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PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Apparently an Aschheim-Zondek test was not performed, at least there is no note in the record to that effect.

At operation a hemorrhagic mass was found in the outer end of the right salpinx, which proved to be an ectopic pregnancy. The fimbriated ends of both tubes were destroyed and scarred — a finding that is consistent with an old inactive inflammatory process. The uterus contained multiple fibroids, the largest, which measured 9 by 5 by 5 cm., being subserosal and placed anteriorly on the right. The intramural fibroids varied from 1 to 3 cm. in diameter. A subtotal hysterectomy and right salpingo-oophorectomy were performed.

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"TURN BACK, O MAN, "

THERE is a doubt today in the minds of many of us how far science can be trusted—a feeling that the cunning with which man has been endowed has betrayed his philosophy and his emotional balance. Our ingenuity, we suspect, has developed far beyond our ethical capacity to guide it, as if a child had released the brakes and engaged the clutch of a machine too powerful and too swift for his control.

It is not a new idea that man, cursed with an obsession for destruction, has been given an inventive genius that far transcends the conservative limitations of his intellect and his conscience. Phaeton drove the chariot of the sun high, wide and handsome but completely off its course until a well directed thunderbolt unseated him, Icarus with his wings of wax, which were in direct competition with

his feet of clay, was probably the mythological inspiration of Darius Green, the car of Juggernaut was built by man and proved to be a man-destroyer, and the creation that Frankenstein introduced made apparently in his own image, turned out to be only his undoing.

There seems to be little in discovery that is good that is not at least counterbalanced by its possibilities for evil. Almost no labor-saving device has been developed that has not had its unfortunate consequences, if only in a weakening of man's moral and physical fiber, just as the old ships of wood with men of iron were supposed to have been replaced by ships of iron manned by men of wood (a comparison, by the way, that recent years have shown to be not entirely true). The benefits that have accrued to man from the invention of the airplane are but a drop in the bucket compared to its overwhelming development as an instrument of destruction.

And now we have the climax-capping discovery of a practical method of unleashing the energy of the atom in a cataclysm of destruction that makes firecrackers of Jove's thunderbolts. It is another discovery of a new instrumentality that will end all wars, as it was instrumental in ending the second world conflict, until the next war begins, when it may easily end man's dominance in a world that he has used so ill. We might entertain the thought now, and seriously, that what the world needs most at present is a strict limitation on the excesses of technology and the renaissance and dissemination of certain poorly remembered spiritual and humanitarian values. Man might then conceivably become more worthy of his continued existence on this sorely tried planet.

Once again, and with feeling, we might recall the hymn written by Clifford Bax so soon after the ending of the first world war

Turn back, O man, forswear thy foolish ways
Old now is earth, and none may count her days,
Yet thou, her child, whose head is crowned with flame,
Still wilt not hear thine inner God proclaim—
"Turn back, O man, forswear thy foolish ways"

Earth might be fair and all men glad and wise
Age after age their tragic empires rise,
Built while they dream, and in that dreaming weep,
Would man but wake from out his haunted sleep,
Earth might be fair and all men glad and wise

Earth shall be fair, and all her people one,
Nor till that hour shall God's whole will be done
Now, even now, once more from earth to sky,
Peals forth in joy man's old undaunted cry —
"Earth shall be fair and all her folk be one!"

MASSACHUSETTS TO PROVIDE BLOOD AND BLOOD DERIVATIVES

ELSEWHERE in this issue of the *Journal* the Massachusetts Department of Public Health announces the initiation within the next few months of a civilian blood and blood-derivatives program. An attempt will be made to furnish the citizens of Massachusetts with blood plasma and other blood products without cost, on the same basis as anti-serums and vaccines. There is no doubt that such a program will be of the greatest value, and like undertakings have already been started in other parts of the country. A similar purpose is being accomplished in certain localities by the encouragement of blood banks in general hospitals or in institutions under the supervision of local or state health departments. Such blood banks, however, are not, as a rule, able to process the many fractions of human blood that are now called for by the clinicians. Proper authorities should have some control over these blood banks to ensure adequate provisions for sterility and a personnel trained in blood grouping and processing. It is also important to make provisions for preventing the transfer of disease by means of transfusions. Syphilis, malaria and homologous serum jaundice (infectious jaundice) are among the diseases that may be transferred, and under certain conditions, sensitization to various allergens may be transmitted.

The methods of processing blood derivatives have progressed to a point where large-scale production has become feasible and has already been put into effect. In a large measure, this has been due to the splendid accomplishments of workers at the Harvard Medical School under the guidance of Dr Edwin J. Cohn and by their many collaborators throughout the country. The Red Cross has also worked out practical methods of large-scale collections of blood to supply the processing plants. No doubt the continuation of a program such as the one contemplated by the department will permit

all these workers, as well as those in the Division of Biological Laboratories, to continue the development of blood derivatives and to study their uses and applications. Plasma, albumin, immune globulin, fibrin foam and other by-products have already proved useful in medicine and undoubtedly other valuable derivatives will eventually be devised.

A number of other factors are involved in any large-scale program for providing blood and its derivatives, and these must be satisfactorily disposed of before the plan can become well established and can reach a high state of efficiency. From the point of view of the general public, there is a good deal of spade work yet to be done to interest people to give blood now that the incentive of patriotism that served to bring donors to the Red Cross centers has been removed. A new approach and other publicity methods will be needed to assure the number of blood donations that are necessary to make a state-wide program workable. At present, some persons supply blood to hospitals because of their interest in the health and welfare of their relatives and friends, whereas others do it because of the financial reward.

There is also a need to inform the general practitioner about the values and use of the various blood fractions. Under the stimulus of war, plasma and other blood derivatives became readily available to the armed forces and were freely used. It is now recognized by most authorities that plasma is not an adequate substitute for whole blood but that it is useful as an emergency measure for the replacement of blood volume. Indeed, the continued use of plasma or plasma substitutes alone may be harmful in some cases, such as those of severe and prolonged sepsis and of blood loss. Furthermore, there may be a tendency for a physician to rely too much on the blood derivatives in certain types of conditions to the exclusion of adequate diagnosis and treatment of the underlying disease, which may be a severe infection requiring a specific anti-infective agent or a condition demanding surgery. The Massachusetts Department of Public Health, working in co-operation with the Massachusetts Medical Society, is preparing material for the education of the profession in the uses and abuses of the fractions of human blood.

Until such a time as the state program is prepared to supply whole blood or resuspended red cells throughout the Commonwealth, the public must be encouraged to continue to supply hospitals with sufficient donors to keep their blood banks solvent. With a wide community program, the relatives and friends of patients, who, in the past, have been largely responsible for the successful operation of these blood banks, may lose the urge to make blood donations. Even in the absence of such a program, the hospitals have had great difficulty in keeping their blood banks supplied. Furthermore, hospital patients are usually in greater need of whole blood than they are of plasma, as has been found in handling battle casualties.

The successful operation of a blood bank on a state-wide basis in Michigan for a period of more than two years has proved that it is possible to conduct such a project for the benefit of the public. The Massachusetts program, however, is more extensive in that it supplies not only plasma but also all the fractions of human blood. Such an ambitious program will dig deeply into the public purse. The Hyams Trust has made available to the department a building costing \$176,000 for the processing of this blood, and the Legislature has appropriated \$174,000 for the equipment and operation of the laboratory, but the maintenance of the program will require appreciable annual appropriations by the Legislature. There is no question that such an investment for the residents of Massachusetts is worth while, but the success of the venture demands the co-operation of physicians and the public—the latter both as taxpayers and as donors.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CIVILIAN BLOOD AND BLOOD- DERIVATIVES PROGRAM FOR MASSACHUSETTS

Within the next few months Massachusetts will offer its citizens a new and striking public-health service, when the Department of Public Health begins distribution of blood plasma and other blood products without cost on the same basis as serums and vaccines.

The experience of World War II has tremendously increased the knowledge of the uses of human blood and its derivatives. Among the outstanding of these

developments is the separation of blood plasma into its various fractions, a process developed at the Harvard Medical School in close collaboration with the Division of Biologic Laboratories of the Department. The application of blood and its products in civilian medical practice will be greatly extended as a result of the increased knowledge that has been gained, and it is fortunate that the department can count on a large group of civic-minded persons who now know that they can contribute to the welfare of their fellow man through blood donations.

To make possible the statewide use of such a vital resource as human blood, the Department of Public Health has organized a program that will include the following: collection of blood donations as donor programs are organized by civic or other groups in various communities, processing of the blood to the various fractions of known value, such as plasma, albumin, gamma globulin, fibrin foam, fibrin film, blood grouping serums and other fractions still in the process of development, as well as resuspended red cells and whole blood as soon as suitable methods for their preservation are established, and distribution of these products through recognized channels and in accordance with community contribution of blood donations.

The program will operate as a unit of the Division of Biologic Laboratories. The Antitoxin and Vaccine Laboratory of this division celebrated the fiftieth anniversary of its foundation in December, 1944, and its fifty-first year promises to be one of large expansion. The Legislature has appropriated \$174,000 to equip, staff and operate a blood and blood-derivatives program. The Godfrey M. Hyams Trust, of Boston, has donated \$176,000 to Harvard University for the construction of a modern, well equipped laboratory building in which processing and fractionation of blood and its products can be carried out, as well as other essential procedures.

This program will provide for the citizens of Massachusetts a blood and blood-products service that will include all the advances developed during the war. These products are already known to be of unique value in the handling of cases of surgical shock and burns, in brain surgery and dentistry, in cases of anemia and hemophilic bleeding and in a variety of other surgical and medical emergencies. Some blood fractions are used in the control of measles and certain other infectious diseases. Provision of these products will thus represent one of the greatest steps in the promotion of health and the saving of life that the Department of Public Health has ever undertaken.

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR AUGUST, 1945

DISEASES	RÉSUMÉ		
	AUGUST 1945	AUGUST 1944	SEVEN YEAR MEDIAN
Anterior poliomyelitis	128	133	15
Chancroid	1	2	2
Chicken pox	121	192	121
Diphtheria	11	5	8

Dog bite	1008	1025	1064
Dysentery, bacillary	55	18	15
German measles	38	57	34
Gonorrhea	449	426	426
Granuloma inguinale	0	0	*
Lymphogranuloma venereum	1	47	2
Malaria	274	227	281
Measles	76	50	4
Meningitis meningococcal	1	3	1
Meningitis Pfeiffer bacillus	1	2	1†
Meningitis pneumococcal	2	0	0†
Meningitis staphylococcal	1	0	0†
Meningitis streptococcal	0	1	0†
Meningitis other forms	4	4	4†
Meningitis undetermined	1	1	1
Mumps	211	273	157
Pneumonia lobar	93	72	77
Salmonella infections	48	24	13
Scarlet fever	157	197	193
Syphilis	295	393	367
Tuberculosis pulmonary	215	232	263
Tuberculosis, other forms	12	13	24
Typhoid fever	4	3	6
Undulant fever	5	7	5
Whooping cough	551	261	429

*Made reportable December 1943
†Four year average.

COMMENT

Anterior poliomyelitis cases for August markedly exceeded those for July but were slightly fewer than the number of cases in August of last year, which was 133. It appears that our experience with poliomyelitis this summer is similar to that of 1944.

The enteric diseases were prominent in August. Salmonella infections were reported more frequently than in any month since 1937. Bacillary dysentery, which increased from 1 case in June to 44 in July, still remained high. Typhoid fever, of which there were no cases in July, appeared on the scene again, though in number less than half the seven-year median.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Actinomycosis was reported from Falmouth, 1, total, 1.

Anterior poliomyelitis was reported from Abington, 1, Acton, 1, Athol, 2, Barnstable, 1, Becket, 2, Belmont, 4, Beverly, 3, Boston, 25, Braintree, 1, Cambridge, 1, Chelsea, 2, Chicopee, 3, Concord, 1, Dedham, 2, Deerfield, 3, East Bridgewater, 1, Falmouth, 1, Gardner, 2, Gloucester, 8, Greenfield, 2, Hinsdale, 1, Holyoke, 3, Ipswich, 1, Lanesboro, 1, Lexington, 1, Malden, 8, Marblehead, 2, Medford, 2, Melrose, 2, Nahant, 1, Newton, 2, North Adams, 2, North Reading, 2, Norwood, 1, Orleans, 1, Peabody, 1, Pittsfield, 1, Quincy, 2, Reading, 2, Revere, 1, Salem, 1, Saugus, 1, Shirley, 1, Somerville, 3, Springfield, 4, Swampscott, 1, Wakefield, 1, Wales, 2, Wareham, 1, West Springfield, 1, Westboro, 1, Westfield, 1, Westwood, 2, Winthrop, 2, Woburn, 1, Wrentham, 1, Yarmouth, 1, total, 128.

Diphtheria was reported from Boston, 3, Cambridge, 2, New Bedford, 1, Newburyport, 1, Norwood, 1, Reading, 1, Somerville, 1, West Bridgewater, 1, total, 11.

Dysentery, amebic, was reported from Camp Edwards, 5, total, 5.

Dysentery, bacillary, was reported from Amesbury, 1, Belmont, 3, Camp Edwards, 1, Foxboro, 1, Foxboro (State Hospital), 8, Framingham, 1, Peabody, 1, Pittsfield, 1, Waltham (W. E. Fernald School), 2, Worcester (state hospital), 35, total, 54.

Hookworm was reported from Camp Edwards, 3, total, 3.

Lymphocytic choriomeningitis was reported from Townsend, 1, total, 1.

Malaria was reported from Andover, 1, Bedford, 1, Boston, 7, Brockton, 2, Camp Edwards, 42, Cushing General Hospital, 2, Haverhill, 1, Lawrence, 1, Newton, 1, Norwood, 1, Quincy, 2, Saugus, 2, Waltham (regional hospital), 3, Watertown, 1, Woburn, 1, Worcester, 1, total, 69.

Meningitis meningococcal was reported from Boston, 3, East Bridgewater, 1, Southbridge, 1, Springfield, 1, total, 6.

Meningitis Pfeiffer bacillus was reported from Springfield, 1, total, 1.

Meningitis pneumococcal was reported from Lawrence, 1, total, 1.

Meningitis staphylococcal was reported from Attleboro, 2, total, 2.

Meningitis, other forms, was reported from Boston, 3, Everett, 1, total, 4.

Meningitis undetermined was reported from Braintree, 1, total, 1.

Salmonella infections were reported from Amesbury, 1, Boston, 2, Cambridge, 2, Danvers (state hospital), 1, Lynn, 1,

Malden, 1, Quincy (private school) 36, Saugus, 1, Stoneham 1, Ware, 1, Weymouth, 1, total, 48.

Septic sore throat was reported from Amesbury, 1, Boston 7, Haverhill, 1, Lynn, 1, Merrimac, 6, Norwood, 1, total, 17.

Tetanus was reported from Chicopee, 1, Worcester, 1, total, 2.

Trichinosis was reported from Andover, 1, Boston, 1, Cambridge, 1, total, 3.

Typhoid fever was reported from Chicopee, 3, Framingham, 1, total, 4.

Undulant fever was reported from Deerfield, 1, East Brookfield, 1, Gloucester, 1, Somerville, 1, Whately, 1, total, 5.

CORRESPONDENCE

NATURE'S CORRECTIVE

To the Editor Wars do not happen. Whether local or foreign, their cause is inadequate human thinking and behavior.

For years there has been abroad in the world the notion that somehow character, culture and contentment can come through the multiplication of machines. For several generations the selfish lust for comfort in excess of biologic needs and sanctions has led us to make more and more things faster and faster in order that life might become easier and easier. This had little regard for the ancient, unchanging and inflexible laws of Nature within which man must live if true progress is to be made. Like all animals man has limitations,—physical, mental and emotional,—which, when overstepped, invite Nature's intervention to restore her everlasting balances.

History shows and Nature knows that the character changes brought on by heedless easy living so poison human relations that, sooner or later, the resulting emotional conflicts spill youthful blood. And the reason why the war just ended was the greatest emotional explosion in history is that our sleepless machine-made devices, especially those used for the rapid interchange of indigestible ideas, have simultaneously deluded, frightened and embittered widespread populations.

Nature's methods are slow, adapted to man's limited abilities, and solicitous of the long-distance welfare of the species. Machine methods are swift—too swift for the sound evaluation and control of their many complex and often pathologic consequences, including corrupting concepts of "labor," "leisure," "security" and impulsive "planning."

Thus the picture contains more than the fantastic physical mass production of machines, with their domestic and foreign social, political and economic complications and repercussions. We have also mass production of frustrations, jealousies, dislocations, fears and follies and a vast train of unmanageable emotional and other distempers, which twice have been blazed into world war. The common man, forsaking valuable ideas and goaded by his machine-made emotions and unbiologic illusions, resorts to violence—each nation according to real or fancied necessity. And once again Nature steps in to invoke her bleak rule governing survival of the fit.

When the excessive mechanization (including political and economic) of society creates such unnatural, swiftly changing and confused surroundings that distortion and deterioration of standards and values result, man's limited biologic equipment (including his mental, moral and spiritual potentialities) is unequal to the task of making rational peaceful adjustments. This seems to be a law of diminishing cultural returns.

The "Great Push Up" cannot work its magic, and the principles and practices of true Christian democracy are not likely to prevail in societies shadowed by the astronomic complexities wrought by machine-made delusions and emotions, brewed in highly abnormal urbanized industrial economies.

Meanwhile we still live in an orderly world. Above the tumult, strife and sadness, Nature goes her just and appointed way. That some should perish is the price society must pay for venturing too fast, too far and too selfishly on new frontiers. Having misused our talents and liberties, Nature seeks through measured disciplines and purges to return man to simpler faiths and enterprises, better fitted to his understanding and control.

Finally, the unquenchable thirst of the human soul for freedom—physical, mental and spiritual—again moves men to recapture and reorient, according to their lights, those ideas and ideals under which they wish to live. Thus do men, serving Nature, strive to compose the increasingly emotional and unmanageable world that their imperfect powers have built.

A E P ROCKWELL, M D

Shrewsbury, Massachusetts

DEPRIVATION OF LICENSE

To the Editor At a meeting of the Board of Registration in Medicine held on September 12 the Board voted to revoke the registration of Dr Abraham Freitag because of gross misconduct in the practice of his profession, as shown by his recent court conviction.

H QUIMBY GALLUPE, M D, *Secretary*
Board of Registration in Medicine

State House
Boston

AN APPEAL

To the Editor This is a copy of a letter that will appear this month in the *Hippocrat*, the official publication of the Hampden District Medical Society. Can anything be done about it?

To the Editor To those of us who gripe about an income tax, to those of us who are so busy calling ourselves specialists that we cannot attend to night calls and general practice any more, to those of us who crab because so-called "lesser men" are getting all the business and to those of us who would momentarily forget that a hundred men from this area have not only risked their skins but have been working for about \$100 a week for several years past while two hundred of us have been living in safety and comfort, I submit this copy of a letter that I received today from a very essential man who waived a disability and who is, and always has been, as humble in his medical career as he is competent.

After thirty-seven days at sea we finally landed here in the Philippines, living in tents in a large staging area with all its attendant discomforts—crowded tents, poor food, no cigarettes unless you buy them from the natives for \$4.00 a carton and a half-mile walk to the nearest latrine and, to top it off, steaming heat alternating with torrential downpours. We are scheduled to stay here six weeks, and then on to Japan. Quite a future now that the war is over. You are acquainted with the red tape of the Army, and it may be a long time before any of us get home. There are many medical officers in the outfit who have spent eighteen to thirty-six months in the ETO. It is all so unfair, to them especially, since we know of many medics in the states who have never been overseas. As for myself, I fail to see what use I can be to the Army now that there are no more battle casualties, for which I thank God. While the war was on, I did not complain, for I knew that I had a job to do, but now I and countless others have plenty to gripe about. What little news we get from the states is too confusing to give us much hope, the wrangling between President Truman and the Senate regarding the soldiers makes us wonder whether the people at home realize what three or four years in the Army can do to a former civilized human being. You may recall that I was on the essential list at my hospital but asked them to release me, since I felt it my duty to join the Army. Now, after three years, I feel that I have made my contribution. It would make you sick to see the thousands of medical officers sitting around in these staging areas with nothing to do and no work for the near future, and yet the Army holds them despite the crying need for doctors at home.

I may as well come to the point. Is there anything you can do either through the Massachusetts Medical Society or by your own efforts to hasten release from this futile existence? Most of the doctors are working on their congressman and on Senator Mead, of New York, who apparently champions our cause. For the

sake of old times, I should eternally appreciate any thing you might accomplish to return me to the civilized type of living to which I am entitled. Remember me to the others, and my best to you and yours.

This particular doctor is the most competent man in his field in Western Massachusetts. He is a thorough gentleman and one of the finest men of my acquaintance. One can readily see that he is not politically minded, yet his heart must be in turmoil or he never would have committed himself to a letter such as this. Although some will suspect whence this letter comes, I shall refuse to divulge the name until such time as I may meet a sincere effort for his release. Incidentally he does not speak for himself alone.

W A R CHAPIN

BOOKS-RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Essentials of Allergy By Leo H. Crip, M.D., assistant professor of medicine and lecturer in immunology, School of Medicine, University of Pittsburgh, chairman, Department of Medicine, Montefiore Hospital, member of senior staff in medicine, Presbyterian and Passavant hospitals, Pittsburgh, and consultant in allergy to the Medical Service, United States Veterans Administration. With a foreword by Robert A. Cooke, M.D., chairman, Committee on Education, American Academy of Allergy. 12°, cloth, 381 pp., with 42 illustrations and 1 plate. Philadelphia: J. B. Lippincott Company, 1945. \$5.00.

This manual is intended for the use of the medical student and the practising physician. The subject matter is dealt with in outline form, resulting in conciseness and clarity of expression. The work is made up of two parts, the first deals with the basic immunologic principles of anaphylaxis and allergy, and the second, comprising most of the text, discusses the diagnosis and treatment of allergy and the various allergy entities. The manual concludes with chapters on the diagnostic skin tests and on allergy in children. Case reports are appended to each chapter to illustrate essential practical considerations. In controversial issues the view that is most readily acceptable is adopted for teaching purposes. The printing is good, on good paper, with a good type. There is an adequate index, and selected bibliographies are appended to each chapter. The manual should prove useful within its intended scope.

Patients Have Families By Henry B. Richardson, M.D., associate professor of clinical medicine, Cornell University Medical College, attending physician, New York Hospital, and visiting physician, Bellevue Hospital. 8°, cloth, 408 pp., New York: The Commonwealth Fund, 1945. \$3.00.

Physicians are beginning to realize that patients cannot be considered apart from their families and their communities. Their illnesses may be profoundly affected by the stresses and strains of these human relations. This book is based in large part on a family study conducted by a number of New York organizations seeking a better understanding of the family as a unit in medical care and of the implications for treatment. Dr. Richardson tells in nontechnical language of characteristic family patterns that appear in connection with different illnesses, and indicates their significance to the physician in diagnosis and treatment. He demonstrates the advantages of pooling the different services of the hospital and of the community to get a complete picture of the family, and shows how such co-operation can improve medical practice. The book should be in all medical, hospital and social libraries and should be of importance to all physicians and to others who are interested in family and social welfare.

(Notices on page vii)

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THE GREEKS HAD A WORD FOR IT*

BEN AMES WILLIAMS

CHESTNUT HILL, MASSACHUSETTS

AMONG the lesser deities worshiped by the ancient Greeks there was one who wore the beard, the ears and the horns of a goat. In fact, his imaginary aspect largely shaped our subsequent conception of the Devil. According to the Greeks, when this creature appeared suddenly to human beings, he awoke in them a storm of sudden fear. They called him Pan, and called the fear that he evoked "panic."

In this respect, in this trait of provoking panic or fear, the great god Pan has his prototype today, but we no longer worship the lesser gods, so we do not call him Pan. We call him "Doctor," and tremble at his name.

The prospect of summoning a doctor, for himself or for one of his family, frightens almost every layman. This may be—and doubtless is—absurd, but the fear is deeply rooted in the past—and the physician himself is its father. The old witch doctors who catered to savage tribes used masks, incantations and every imaginable sort of humbug to frighten their prospective patients. To observe their antics was to conclude that they believed a patient thoroughly frightened was already half cured. It is too often true today that doctors appear to proceed on the same theory. Their actions suggest that they believe a good fright beats all the drugs in the pharmacopoeia.

Doctors do not sufficiently realize the fact that their patients are frightened, and do not give enough attention to the particular branch of pathology that involves a study of the emotions. I know that you have courses in what is called "psychosomatic medicine,"—the phrase alone, like most medical phrases, is enough to frighten the average patient,—yet I suspect that it is a doctor, not a patient, who gives those courses, and this may reduce their usefulness. During a recent brief wait in a doctor's office I took off his shelves a book dealing with some general principles of private practice, and found in it a chapter on psychiatry. That chapter dealt with mental aberrations resulting from drunkenness and from syphilis but with no other mental twists at all. Yet I suggest to you that every patient, sick or well, is

in greater or less degree a psychoneurotic—and should be so considered by his doctor.

If this is true in no other respect, you may be sure he has a fear psychosis, for he is afraid of you. I suggest to you that in this respect your education has been neglected, that you have been insufficiently warned of the importance, when you begin to practice, of healing first of all your patient's fear.

Of course I understand—and so do you—that your medical education is just beginning. If you are wise, you will accept the fact that it will never be complete. You have learned something about the use of medicines, have witnessed or have performed dissections of dead and of living flesh and have had some contact with the sick. But your first private patient will extend your education, and—if your mental capacities endure that long—so will your last. In fact, I suspect that every medical school should have a course of lectures given by patients! Certainly any doctor, after having once been ill himself, is a better doctor afterward.

The lesson that every doctor most needs to learn is that his patients are afraid. They have heard so many dreadful tales beginning with the formula "He never had a sick day in his life till one Friday he felt a little queer and went to a doctor, and do you know—" If they are of my generation they have heard their elders say ruefully, "Yes, he's going to have an operation, and you know the knife is the knife." It is, basically, not the knife the layman fears, it is that he will die, as the phrase goes, "on the table." I believe that deaths during an operation are decidedly rare. If every prospective operative patient—and his family—knew this, if he were assured that, no matter what the long-range results might be, he would survive the actual operation, his fears would be tremendously relieved.

There are so many of these fears. The patient is afraid of what the doctor will tell him, and as a result he often puts off seeing a doctor at all till it is too late to help him. Basically this is not fear of what the doctor may discover, but fear of the mysterious and terrible and godlike creature himself. Your patients will be afraid of you. Of course if you

*A George W. Gay Lecture on Medical Ethics presented at the Harvard Medical School May 15, 1945.

are young and handsome and your patients are neurotic women, this fear may be replaced by another emotion, but the normal person, finding it necessary to see a doctor, is frightened. I believe that some study has been made of the body's chemical reaction to emotions. Those of you who incline to a life of research might go far in that field. If, for instance, ulcers of the stomach are caused by an excess of hydrochloric acid in the digestive fluid, what emotions produce that excess? If you always remember that a patient who comes to you for diagnosis is afraid, what allowance must you make, in appraising his symptoms, for the chemical effect on him of that fear? What steps can you take to allay it, to allay not only his fears, but those of the well people who love him?

For of course the wise doctor will always remember that it may be quite as easy to make a well person sick as to make a sick person well. The recital of symptoms may produce them — in the well or in the sick. To suggest a parallel in which the conscious replaces the subconscious suppose a man goes to a lawyer, says, "I want to sue John Doe" and recites his grievance. The lawyer says to him, "You have no case." He asks, "Why not?" And the lawyer replies, "Well, to have a good case, John Doe must have done and said so and so, and you must have done and said so and so." The client, thus informed of what his evidence should be, will go into court and testify to the exact state of affairs thus suggested to him. He will soon come to believe that he is telling the truth. In the same way the patient to whom symptoms are suggested will as often as not imagine he has them.

Probably a large proportion of you are planning to become specialists — and you have doubtless heard of the young doctor who appealed to a wise old physician for advice as to which specialty he should adopt. The old man suggested skin diseases, the young man asked why, and the old man said, "Because anyone who consults a doctor about a skin disease can afford to pay his bill, and patients with skin diseases don't die of them, and they don't get better." I always thought this anecdote amusing till I acquired a little purpura of my own.

Some of you will become specialists. For those of you who do so, the fact that your patient is afraid of you is particularly worth remembering, for he is much more afraid of you than of his family physician. For one thing, you and he are usually strangers, for another, he mistrusts you because he knows that a specialist, like a shoemaker, tends to stick to his last, to his specialty.

I heard an instance of this a week ago. At a certain medical school, specialists came regularly to lecture, and for material to illustrate the points they wished to make they turned to the wards in the available hospital. Once upon a time a psychiatrist came to lecture, found in the wards a patient with a pronounced psychosis and used her as a text for

his discourse. A fortnight later a dermatologist found in the wards a sufferer from numerous skin lesions, and used this patient to illustrate his points. Subsequently an expert on digestive disturbances selected a patient with persistent diarrhea, and since she had spent twenty years in China, the students made elaborate studies of her stools to discover the cause. No one was struck by the coincidence that the patient who was used by each man as an object lesson was the same person until a general practitioner, an old country doctor, happened on her and after a glance at her history said in some excitement "Why here you have something really remarkable. Dementia, dermatitis, diarrheal. This woman has pellagra." Which was true.

This tendency to wear blinders, to see only his own field, is one of the specialist's handicaps. His achievements are the more remarkable because he struggles against so many of these handicaps — handicaps rooted in his own psychology, handicaps arising from his inevitable ignorance of his patients, handicaps arising out of the fact that he knows his own field — or that he doesn't!

The increasing tendency toward specialization has led medicine to follow the example of industry, — to establish a production line. The human chassis, on a belt conveyor, passes under the eyes of a regiment of specialists, and one does this and another does that, each restricting himself to his particular field. And as though the mechanic who affixed the bumper thought he had built the car, each doctor when the patient recovers may secretly assure himself that he and he alone accomplished the cure. For the specialist tends to find in his own specialty the source of every human ill. To the dentist, it is the teeth, to the oculist, it is the eye, to the gastroenterologist, the stomach, to the cardiologist, the heart. Just as the successful businessman comes to think of his very own business — the manufacture of some particular soft drink, the production of rivets, the distilling of alcohol — as the foundation of our economic structure, so the specialist may come to believe that in his field lies every healing virtue. In my home county in southern Ohio a hundred and fifty years ago a surgeon of parts — he more than once successfully trephined skulls with a cutting instrument that he himself had made at the nearest blacksmith shop — was not so well equipped in the medical field. Once upon a time he was called to attend a little girl in an emergency while a more informed physician was being summoned. When the other doctor arrived he found the patient in convulsions, and could not guess their cause, until his predecessor explained "Oh, that's because I gave her strychnine. I knew it would give her fits, and I'm death on fits!"

The specialist, discovering in his patient familiar symptoms, may give a secret shout of joy at finding himself on ground he knows. For the specialist like the rest of us, often flounders in ignorance. I

never submit myself to a doctor's mysterious thumpings and tappings without remembering the old railroad man, fifty years on the same job, to whom for long service a gold medal was to be presented. A special train carrying the president of the railroad and other high officials pulled up to the remote mountain siding where the old man worked. The president delivered his speech, the medal was presented, and then the old man was asked to tell something of his years of service. He had had for fifty years, he said, the same job. When a train stopped at the siding he took a long-handled hammer and went up one side of the train and down the other, tapping every wheel. "Why?" the president asked, and the old man scratched his head and said, "Well, I never did know!" That sounds ridiculous, but as a matter of fact he did not need to know, for if to one of his tappings the wheel had responded with the wrong resonance, he would have recognized the fact that something was wrong.

I sometimes suspect that any layman who approached a patient's bedside with a cheerful and reassuring manner and the conventional equipment in his bag, who went through the routine — finger on pulse and watch in hand, "Let me see your tongue, say 'Ah,'" attach a blood-pressure apparatus, listen with a stethoscope, tap here, tap there — and then said confidently "Why you're fine. Stay in bed a couple of days and drink a lot of water" would make a highly successful practitioner — if he had sufficient common sense, when he encountered a person who was really ill, to recognize that fact and summon a consultant.

I have suggested that specialists may sometimes be too ready to see in every patient a sufferer from the ailment that is his specialty. It is perhaps a defensive psychology — for doctors are psychiatric cases too — that sometimes leads specialists to the opposite extreme. I know a man with gout who went twice to one orthopedic specialist and four times to another, complaining each time of a sore and swollen foot, before gout was even suggested! I know another man who had a sore throat and went to one doctor after another, including three throat specialists, losing his tonsils here, his adenoids there and forty pounds of weight in the process, before I told him he had thyroid disease — of which he was promptly and permanently cured.

In addition to the basic handicap of being a specialist, the specialist must overcome other disabilities. His greater knowledge may lead him contemptuously to dismiss the suggestions of the patient, yet the patient is often his own best doctor. I understand that the human body commonly manifests a sound instinct for self-defense. Does not the omentum, for instance, tend to seal off an intestinal perforation? If the jugular vein is cut, do not other veins take up its burden? If an eye or a kidney or an arm is lost, does not the remaining member rise to the occasion? The brain is an organ

as intelligent as the omentum, or the jugular vein, or the kidney, and the patient's brain may conceivably know better than any specialist what the patient's body needs. So, no matter how certainly the specialist knows that his patient is wrong, he will, if he is wise, give respectful consideration to the patient's ideas.

This suggests the greatest of the many handicaps under which the specialist labors, for he does not know his patient. Lacking knowledge of the individual, he cannot accurately appraise what the patient tells him. Nor can the patient's own doctor, the general practitioner, pass on his knowledge to the specialist. He may know, yet not know how he knows. There are so many intangibles in medicine. Pain is a symptom, but what is pain? How measure it? I know a man who had an abscessed tooth that broke when an attempt was made to extract it, and who then allowed the dentist to drill out the fragments without using an anesthetic. I know another who is deterred only by shame from demanding novocain for an ordinary dental prophylaxis. Obviously, pain has one meaning for one of these men, another for the other. When a man tells his doctors that something hurts, his family doctor knows — although he cannot always say — what the man means, but the specialist does not.

So the specialist has all my sympathy. I, as a patient, — or as a member of the patient's family, — have had occasion to wish I had more of his. Once upon a time my younger son, while sliding downhill on a sled, received a hard blow on his head. Our general practitioner stitched up his scalp and the swelling subsided, but a month later, touching his head in a casual caress, I discovered a depression in his youthful skull. I called our doctor. He said comfortably, "Yes, yes." It was as though he had known or expected just this development. He assured me that there was no cause for alarm, but since I was not reassured, he suggested that I see Doctor So-and-So. Doctor So-and-So made elaborate tests and said the youngster was all right, but he took x-ray films to make sure, and told me to come in three days later — they were three long days, believe me — to hear the verdict. When I appeared at his office and gave my name, his nurse said to his receptionist, "Dr. So-and-So wishes to see Mr. Williams personally." She ushered me into an examination room with shattered skulls in the cabinets around the wall, with no chair and with nothing to read, and shut the door and left me there for forty minutes. Then Dr. So-and-So came in and said everything was fine! Now, I was glad to know that everything was fine, but to keep me waiting so long, under such circumstances, for that information was evidence of an astonishing insensibility on the part of the doctor. Nor was he an exceptional case. There was an occasion when another doctor was to telephone me at a certain hour, the verdict of the pathologist on a bit of tissue

submitted for examination. He was three hours late in doing so, and when I spoke of this he said he had forgotten! I could cite many equally thoughtless instances, but the point needs no laboring.

Yet in such cases the doctor provokes in the patient — or protracts — a storm of fear, and fear is a poison the ill effects of which need to be recognized. Your success in quieting your patient's fear of you and his fear for himself will in many cases do more for him than all the medical knowledge accumulated through the ages. But doctors too often accentuate rather than allay the fears of their patients. They do it by putting on an act! Summoned to the bedside, they hem and they haw, they take pulse and blood pressure with carefully blank faces, they tap here and tap there, sometimes measuring with their spanned fingers or even with a tape to choose the next spot to tap, sometimes making mysterious marks with blue crayon on the cringing skin. They press a cold stethoscope against warm flesh and make the patient shiver and twitch. They ask mysterious questions without explaining why they do so. I suppose doctors had asked me two or three score times how often I had to get up at night before I mustered courage to inquire why they wanted to know. And I am not an overly timid man.

When you trot out your paraphernalia and begin your tapping and your listening, do it as though it were a matter of form — and never let the patient discover in you any slightest surprise. I stood one day in front of one of these arrangements that allows a doctor to watch what happens when the patient gulps down a tasteless white mixture. After one such swallow one of the corps of observation exclaimed, "That went almighty fast!" I am still wondering what significance attached to the speed with which that beverage went wherever it went — but I have never dared ask.

Doctors seem to wish to be mysterious. They use long words for simple things. They write prescriptions in hieroglyphics over which after the doctor is gone the patient and his family puzzle helplessly. They call a consultant and mutter and mumble with him, and then go into the hall — sometimes in the patient's sight — and whisper long together. Then in tones excessively cheerful they assure the patient that he's just fine, and they depart, and the patient and his family are left to tell each other over and over that there is nothing to worry about — and to think to themselves "There must be something they haven't told us! Did you notice how solemn they were?"

I continue to refer to the patient and his family, for a doctor actually treats not only the patient, but those around him. The obstetrician who said he had never lost a father may have amused his listeners, but he betrayed his own complete ignorance of the extent of his responsibilities.

And these responsibilities are heavy. Not enough

heed is taken by medical men of the ease with which well persons may be made sick. There are mental as well as physical contagions. When measles or scarlet fever runs through a family of children, the doctors find an easy scientific explanation when a husband during his wife's pregnancy has morning sickness, they only smile. A doctor who read this manuscript protested that my simile was a poor one: that I compared the results of a spreading bacterial infection with an emotional situation. But there are emotional as well as physical infections. If you doubt this, read *Psychology of the Crowd*. Hitler spread an emotional infection through an entire nation.

And emotional infections may produce physical ills. Many a man, hearing a list of symptoms, imagines he has them, and the imagined may become the real. I knew one student here at Harvard Medical School who was for a while convinced that he had hydrophobia. It is true he did not contract hydrophobia, but one of his lay friends read this student's textbook on stomach ulcers, developed all the symptoms and consulted a doctor, who put him on a strict dietary regime. If service in the Army had not filled his mind with other matters, he might have become a confirmed hypochondriac.

The human imagination is a powerful force, and it is easily stimulated into activity. The wise doctor, when he puts a question, will remember that the patient is eager to give expected and pleasing replies, eager to placate in every way this doctor of whom he is secretly afraid. So he will ask his questions in such a way that the patient cannot guess the desired answer. And of course, to every reply, no matter how ominous, the wise doctor comments "Fine! That's good!" The first time I had a life-insurance examination the doctor took my blood pressure, smiled approvingly, said "Excellent" and went through the rest of his routine. Then he said, "Now I'll make the second reading." He took my blood pressure again, and grinned. I asked the joke. "It was 184 the first time," he answered. "It's 117 now." My son recently had a physical examination for promotion in the Navy. His blood pressure was high, he was told to come in again. The second time the doctor took his blood pressure, shook his head and said, "A hundred and forty-five." Five minutes later he took it again, it was 180. He laughed and said "Well, we'll ignore blood pressure in your case. It's obviously not a reliable indication of anything. You're scared of doctors, that's all." That was a wise doctor.

Of course some patients, discovering this terror in themselves, arm themselves against it. I knew a woman who at sixty-six consulted a doctor. He found her blood pressure astronomically high and ordered her to bed under penalty of an early demise. She said "Fiddlesticks!", spent her next twenty years in active enjoyment of life — her favorite summer recreation was digging dandelions out of

her lawn — and never again called a doctor until she was eighty-seven years old I am sure it was only coincidence that after fourteen months of solicitous medical care she died

Your patient is always afraid of you Before you start your scientific tests, do all you can to reassure him Your apparatus, you know, will increase his terror, just the sight of it If he's a man, explain it to him, show him how it works, tell him its mechanics I know a man with sensitive teeth who in the dentist's chair sometimes holds a mirror so that he can see what the dentist is about Without the mirror, the dentist's drill feels as violent as one of those air hammers with which burly men rip up street pavements, the patient's tongue assures him that the cavity the dentist has excavated is enormous But the mirror tells him the truth, quiets his fears — and helps him to forget his pain

Interest your patient in the mechanics of your work, and if he is a man he will forget his fear of you With women patients this is not so important Just as men are more modest than women, so are they more imaginative and more easily frightened Women are more interested in the doctor than in his procedures And they are not so likely as men to be afraid Matters of life and death are commonplace to them, they face these mysteries more calmly

In a large proportion of cases, the good that the doctor can do the patient is determined within a few minutes after their first meeting If you are to free the patient of his fear of you, if you are to win his confidence and if you are to enlist his co-operation, these first moments are vital Mistakes made then are hard to remedy The most successful doctor is the one who supplements his professional competence with what salesmen call a good approach For before a doctor can do his best, he must sell himself to the patient, must lead the patient into such a mental attitude that he will get well to please his doctor — or to disappoint him Tell one man he is going to die, he may retort, "I'll be damned if I do" and proceed to prove you wrong And the reverse may sometimes be true There are persons so contrary-minded that they will die just to prove that the doctor — who assured them they were all right — did not know what he was talking about! Any doctor of long experience will remember patients who would have recovered if they had effectively wished to do so He will remember patients who seemed determined to die — and did

To treat your patient properly you must within the first moments of your contact with him study the individual himself You must decide how you will treat his mind before you decide how you will treat his body If you are called in as a consultant, before seeing the patient at all it is wise to learn as much as possible about him from his doctor not his symptoms, not his ailments, but what sort of man he is Is he contrary or easily led? Intelligent

or stupid? Calm or excitable? Is he frankly frightened, or does he hide his fear? For you may be sure he is afraid! What is his business? Is he a successful husband, father or friend? Has he had other illnesses? How did he take them?

As a newspaper reporter sent to interview celebrities I used to try to learn in advance something about them — and about their particular field of work — that they themselves did not know If you can know your patient better than he knows himself, — not only physically but psychologically, — you are so much the better equipped to help him

After you have made his acquaintance and have soothed his fears, you will already have begun, by observation, your diagnosis If you have made a good beginning with him, he will by this time be eager to help you Phrase your questions in such a way that you seem to expect certain answers — and do this particularly when the answer you seem to expect is not significant If he then gives you an opposite answer, you may accept it as true, for he gave it reluctantly, believing that you expected an opposite reply and regretting that he must disappoint you But no matter how alarming his answers to your questions may be, you should always appear to find them reassuring, for the most dangerous drug you can administer to your patient is fear

When you reach the stage of prescribing treatment, your first care should be to avoid reawakening the fear that you have sought to relieve As for treatment, never forget that the patient, like the customer, is always right This may not be literally true, but it is true in enough cases to make every wise physician cautious I remember a man who had been operated on for cancer of the rectum and who was thirsty and to whom water was forbidden He took advantage of the nurse's momentary absence, got out of bed, walked down the corridor to the water cooler, drank all he wanted — and thereafter made an astonishingly swift recovery and never had another sick day until twenty-seven years afterward, when a runaway truck jammed him against a store front and crushed his spine — this in spite of the fact that he had had a disease that is ordinarily considered to be incurable

But that is beside the point The point is that he drank a forbidden draft and got better The point is that the patient often knows best what is good for him I remember another man who after some diagnostic procedure — I believe this was an injection of glucose to test his reaction — was told to dress, go downtown, go to a ball game and amuse himself He protested that he felt sick and preferred to stay in bed His nurse, presumably under instructions, insistently kidded him into going — and he collapsed in the subway, and when a taxicab brought him back to the hospital, he was in a condition so extreme that a wheel chair was necessary

submitted for examination. He was three hours late in doing so, and when I spoke of this he said he had forgotten! I could cite many equally thoughtless instances, but the point needs no laboring.

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THE INFLUENCE OF PREGNANCY ON OTOSCLEROSIS*

RICHARD T. BARTON, M.D.†

BOSTON

THE relation of pregnancy to otosclerosis, the indication for abortion and the effect of abortion on the progress of the disease are topics that have rarely been discussed in the English medical literature. The literature in Europe in the last decade has been stimulated and influenced by German attempts to lay down rules for their eugenics courts to regulate this particular disease. In this country, no formal statements have been made on the subject, yet the interruption of a pregnancy complicating otosclerosis is not an infrequent procedure in hospitals.

MATERIAL AND METHODS

All the cases of otosclerosis at the University of Chicago Clinics were studied in conjunction with Dr. Delbert K. Judd. Those reviewed at the Massachusetts Eye and Ear Infirmary were taken largely from the extensive records of Dr. Ruth P. Guilder, of the Winthrop Foundation. This study revealed 133 otosclerotic women who had experienced one or more pregnancies. All these cases had been ex-

It was the patient's first pregnancy and the hearing returned to its previous level after parturition. This phenomenon has been observed in the past. Ashcroft² reports 2 cases of temporary improvement of otosclerotic deafness during pregnancy, one during the first three months of pregnancy only and the other during the last month. In both cases the auditory function returned to its previous level after parturition.

Many authors have blamed the progression of the disease on certain endocrine changes. Such changes taking place in one of the following periods

TABLE 2 Time of Onset of Hearing Loss

TIME OF ONSET	NO OF CASES	PERCENTAGE
During pregnancy	12	20
Immediately after pregnancy (during lactation)	50	51
Six months or more after parturition	17	29
No data	14	
Total	73	

have been suspected during pregnancy, immediately after it (during lactation)^{3, 4} and six months or more after parturition. Table 2 gives the results in this series and demonstrates that the hearing loss commences immediately after delivery in about half the cases. Whether increased deafness six months or more after delivery should be attributed to the pregnancy or to some other inciting agent is open to question.

The fact that the deafness of otosclerotic women is sometimes made worse by pregnancy does not mean that it is always the first gestation that precipitates the hearing loss. Many cases have been unaffected by previous pregnancies, as demonstrated in Table 3. Fialovzky⁵ states that the

TABLE 1 Effect of Pregnancy on Otosclerotic Deafness

DEAFNESS	NO OF CASES	PERCENTAGE
Made worse	73	64
Unaffected	40	35
Made better	1	1
Effect unknown	19	
Total	133	

amined and completely tested to make the diagnosis reasonably certain. There were 19 cases in which for various reasons it was impossible to ascertain complete information concerning the effect of the pregnancies.

RESULTS

The results given in Table 1 demonstrate that nearly two thirds of the otosclerotics studied were made worse by at least one of their pregnancies. The cases listed as "unaffected" were those in which the course of the disease was not appreciably altered by pregnancy. These results differ from those of Schmidt,¹ who stated that in half his cases pregnancy had an unfavorable effect on otosclerosis and that in the other half there was no effect during or after it.

In only 1 case did the hearing improve during pregnancy, and this effect was only temporary.

*From the Department of Otolaryngology, Massachusetts Eye and Ear Infirmary. Presented at the annual meeting of the New England Otolaryngological Society, Boston, February 7, 1945.

†Formerly resident, Otolaryngological Service, Massachusetts Eye and Ear Infirmary.

TABLE 3 Relation of Onset of Hearing Loss to the Number of Pregnancies

PREGNANCY	NO OF CASES	PERCENTAGE
First	51	70
Second	12	16
Third	5	7
Fourth	3	4
Fifth	0	0
Sixth	1	1
Seventh	1	1
Total	73	

damage sustained in the first pregnancy in most cases recedes, whereas that aggravated by later pregnancies usually persists. Among 51 cases in the present series in which the deafness had its onset with the first pregnancy, in only 2 did the damage recede. In all the others the hearing loss was maintained. It is important to note that the

to get him to his room. So the patient may have a sound idea about what treatment he needs.

To the doctor's most persistent psychiatric problem — How much of the truth shall you tell the patient? — there is no complete answer. Yet the better you know your patient, the more wisely you can solve this problem. How much of the truth will you tell a patient with a hopeless case? To be sure, you may be wrong in your diagnosis, but in what seems to you a hopeless case, will you be frank with the patient? Will you tell his family? One doctor of wide experience recently assured me that he never tells the hopeless truth. I have known two people who were killed — their deaths hastened — by being told the truth. One, an old man who had been a granite cutter in his youth, had, through a long life, been proud of the fact that he had never contracted tuberculosis. In his middle seventies he fell ill. I was with him — he was jolly, mentally himself, physically strong enough to walk and talk — when a rural doctor whom he had consulted came into the room and said flatly, "Mr. McC, you have tuberculosis." He never spoke another rational word, and died ten days later. Another, a woman, developed a progressive and incurable ailment, but her life expectancy was ten, twenty or thirty years. Told that she would never get better, she died in three months.

On the other hand, I have known men who were told that their days were numbered — and who lived full and happy lives for many a year thereafter. I think of one man who was given — on condition that he mended his outrageously dissipated ways — a maximum of six months. He decided that virtue was not worth the price, and has continued his excesses through the sixteen years that have ensued since the day sentence was pronounced on him. To decide who shall be told the hopeless truth is a problem impossible of positive solution, but he who oftenest solves it correctly is the best doctor.

Fear is a poison, yet sometimes doctors seem deliberately to provoke fear. It is as though they

were completely unaware of the impact on a patient of their smallest word. A certain doctor, while making a routine examination of a patient who had come for a simple checkup, applied the stethoscope and listened for a moment and then asked gravely, "Has anyone ever told you you had heart trouble?" The patient, naturally startled, said "No. Have I?" The doctor, without replying, turned and left the room. That was a dozen years ago, and no doctor has yet discovered that there is anything wrong with the patient's heart, but the idiotic question left behind it a cloud of shadowy terror that only time dispelled.

In another case the doctor had found puzzling symptoms. The patient spoke of a pain in his head, the doctor laughingly recalled a case of another patient who bewildered doctors for days — and turned out to have a brain tumor! So the patient acquired a new fear.

Another, a woman already in her seventies, broke her hip. When she was, so far as she would ever be, recovered, the doctor said severely "Now you're all right, but there is one thing you must remember. Under no circumstances must you break your hip again!" So he gave her terror to walk with her all her days.

If some of these ridiculous cases seem to you incredible, I can only assure you that they are literally true. And it is the astonishing errors of great men, not the routine follies of small ones, that I have cited to you today.

It is the hard lot of the doctor to know that in the end he is always defeated, his victories at best are temporary. Death he can never finally conquer. But death's ally is fear, and this ally the doctor can defeat. Let him help the patient to conquer fear, and he will win many a skirmish, and if he can never hope to win the last grim battle, he can at least do much to rob that ultimate defeat, for his patient and for the patient's family, of the terror that is its most grievous pain.

in Germany for all indications before and after Hitler. In 1932 there were 34,690 abortions, whereas in 1937 there were only 3891

COMMENT

In reviewing this series, many cases were encountered that contradict most of the above opinions. It is of importance that there were many examples of multiparous otosclerotic patients who suffered a hearing loss with early pregnancies but were completely unaffected by subsequent ones. Therefore, the effect of previous pregnancies is not an accurate index of the effect of subsequent ones. The most striking fact in the entire series was the complete lack of regularity in cases of otosclerosis complicated by pregnancy. No definite rule can be laid

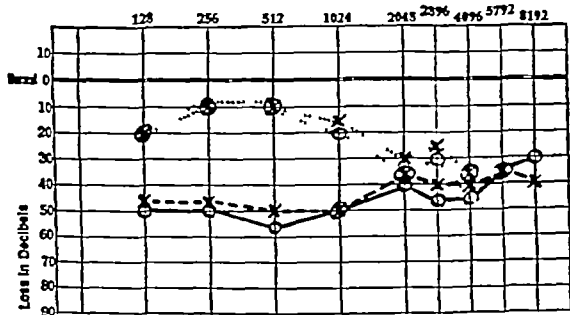


FIGURE 1 Audiogram Taken One Year after Therapeutic Abortion and Sterilization

down concerning abortion until the etiology of otosclerosis is solved — if even then. Torturing tinnitus is an extremely rare by-product of otosclerotic deafness and usually represents a psychotic or neurotic problem. This can be adequately controlled by sedation and psychotherapeutic measures.

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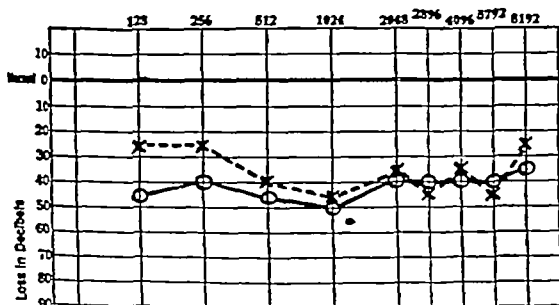


FIGURE 2 Audiogram Taken in the Third Month of Patient's First Pregnancy, Subsequent to Therapeutic Abortion

progression of the deafness. One was a twenty-seven-year-old woman, whose deafness had appeared six years previously, immediately after the birth of her first child. The hearing loss was increased by a second pregnancy three years later. A year following this, the patient was aborted and sterilized by ligation of the fallopian tubes in the second month of her third pregnancy. Her hearing

had not been altered by the third pregnancy and was no worse after the abortion. The patient was told that if she did not have this done, she would become totally deaf. Evidence from this series indicates this to be an unjustifiable prediction. The audiogram taken one year after the therapeutic abortion is shown in Figure 1.

The second case was that of a thirty-seven-year-old woman whose deafness came on gradually,

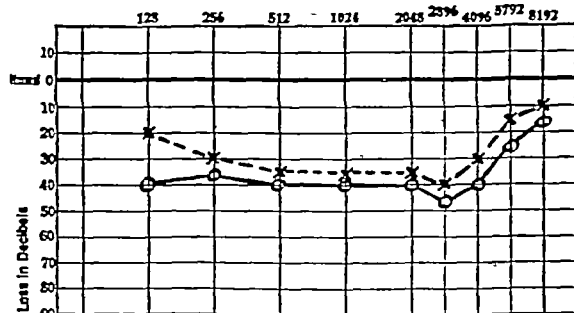


FIGURE 3 Audiogram Taken Two Weeks after the Interruption of the Pregnancy

There is a slight improvement between 4096 and 8192, which was unnoticed by the patient because it is outside the speech range.

commencing twelve years previously. The maternal grandfather had had otosclerotic deafness, but no other member of the family was affected. The hearing loss progressed slowly but steadily. In November, 1940, the patient became pregnant and by the third month of pregnancy developed a marked increase in tinnitus but no apparent increase in hearing loss. An audiogram (Fig 2) was

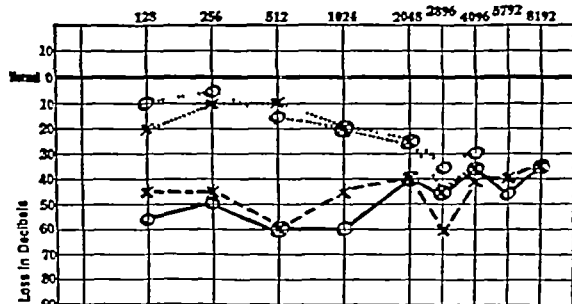


FIGURE 4 Audiogram Taken Eight Months after the Patient's Full-Term Pregnancy and Over Three Years after the One Shown in Figure 2

There was a 15-decibel loss between 128 and 1024 in three years, which probably represents the natural progression of the disease. The patient noticed no hearing loss with either pregnancy.

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hearing may or may not be further damaged by subsequent pregnancies

Blohmke³ writes that the aggravation of hearing loss usually occurs not in the first pregnancy but in a later — second or third — one. He claims that this is especially true in rapidly successive childbearing. Alexander⁶ and Helot⁷ are of a somewhat similar opinion. Table 3 does not corroborate this, but agrees with Stein's⁸ statement that the onset of the ear affection occurs most frequently at the time of the first pregnancy, although several pregnancies may occur without damaging the hearing. There was, however, little evidence in the entire series that the rapid succession of pregnancies was any more harmful to the hearing than were the same number of widely distributed gestations. Many of the otosclerotic patients who were un-

TABLE 4 *Number of Pregnancies in Which Hearing was Unaffected*

NO OF PREGNANCIES	NO OF CASES	PERCENTAGE
One	20	50
Two	12	30
Three	2	5
Four	3	8
Seven	2	5
Eleven	1	3
Total	40	

affected by pregnancy experienced more than one gestation without increased hearing loss (Table 4).

In summary, the tables demonstrate first, that many otosclerotic patients are unfavorably affected by pregnancy. This has long been known and has been observed by many medical writers. Second, that the hearing loss is likely to commence at any time in relation to pregnancy, that is during, immediately after parturition or six months later. Third, that this type of deafness most frequently has its onset with the first pregnancy, although in some cases it begins only after several gestations. Both Tables 3 and 4 indicate the first pregnancy as the one likeliest to affect the hearing (72 per cent). The patient, however, has a 50 per cent chance of experiencing subsequent pregnancies without further progression of otosclerosis.

INDICATIONS FOR ABORTION

The problem of abortion is an extremely difficult one, for many reasons other than conflicting religious views and conflicting political ideologies. The facts that the ability to adjust to deafness psychologically varies with the individual, that otosclerosis — unlike other indications for abortion, such as toxemia, tuberculosis and heart disease — does not endanger the life of the patient and that the effect of abortion on the hearing loss is unpredictable⁹⁻¹¹ make every case in which this question arises controversial. As a result, the literature offers every opinion from one extreme to the other.

There are those who assert that in no case is abortion indicated in otosclerosis. Blohmke, Kummel, Struyken and Quix¹² are among them. They believe that abortion means destroying one life for the health of another. It is their opinion, therefore, that the mother's hearing under no circumstance outweighs the baby's life. Also, Nager¹³ is of the opinion that the ill effects of pregnancy on otosclerosis have been exaggerated. Of his 547 otosclerotic female patients, 264 were unmarried. If, therefore, the influence of childbearing were so deleterious, he reasons that a larger proportion of married women would have been affected. On the other hand, Welty and Brückner¹⁴ contend that all cases of otosclerosis should be aborted. Then there are authors who have taken a stand somewhere between these extremes and have attempted the difficult task of laying down certain conditions under which abortion is justified.¹⁴

Haik¹⁵ states that to propose any strict indications is impossible, but that there are certain cases in which abortion is justified. He places first those in which there has been considerable deterioration or repeated deterioration in several pregnancies. He insists, however, that this should only be done when the exact hearing status of the patient before pregnancy is known. Second, he states that abortion is especially indicated in such cases when the loss with previous pregnancies is such that another would bring on complete deafness. Finally, he mentions as an absolute indication for abortion "a torturing amount of tinnitus with psychic depression."

Goerke⁹ has written that otosclerotic deafness results in an extremely severe damage to the health and that it is a justifiable indication for abortion when it renders the patient incapable of performing her occupational duties, such as teaching. He adds, however, that all alleviation of hearing loss from abortion is probably the result of self-deception, that is, the patient is relieved of uncomfortable noises and a pregnancy neurosis, a result that can sometimes be produced by physical and mental rest alone. Similar improvement is observed in some cases after delivery, as was pointed out by Alexander.⁶

In 1939, Greifenstein¹⁶ was commissioned by the German Government to study this problem. He was instructed to review all the former indications and the clinical evidence for abortion in an attempt to add directives to the law to cover this situation. He concluded that it was impossible to assign strict directives and that clinical consideration would explode any rigid rule. He quotes Marx as writing that "one can never tell that abortion will forestall further deterioration." Greifenstein concludes his paper with the sole statement that much more material needs to be gathered before a clear decision can be given. It is of interest that he compares the incidence of therapeutic abortion

in Germany for all indications before and after Hitler. In 1932 there were 34,690 abortions, whereas in 1937 there were only 3891

COMMENT

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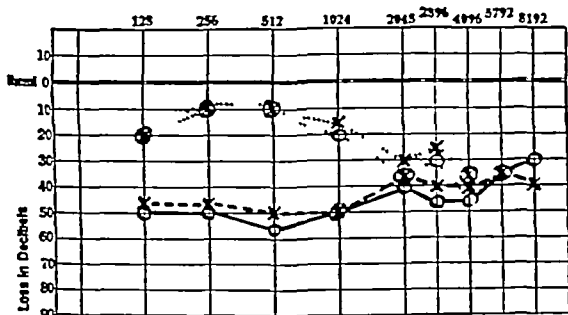


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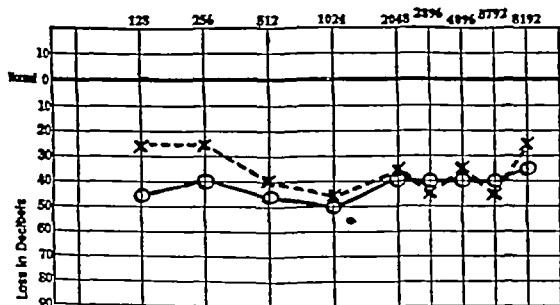


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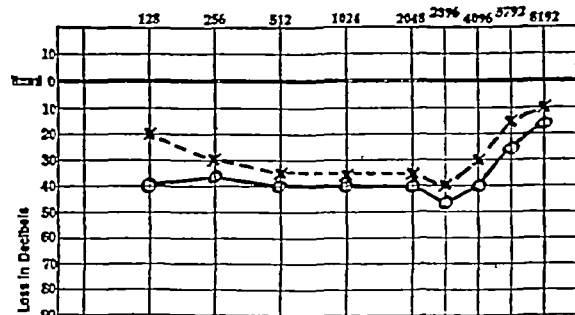


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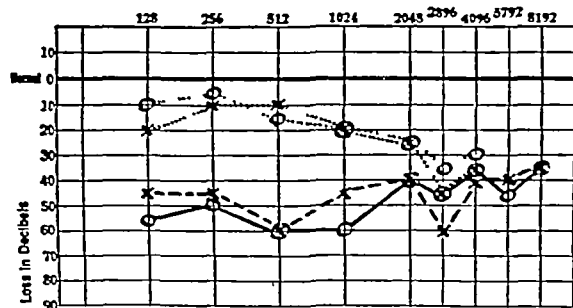


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parturition showed a 15-decibel low-tone loss in the previous three years. The course of this patient's disease was thus apparently not unfavorably affected by a pregnancy and therapeutic abortion or by a full-term pregnancy two and a half years later.

INDICATIONS FOR STERILIZATION

The hereditary nature of otosclerosis is still being debated. The literature contains many clinical studies, such as the latest ones by Weber¹⁷ and Schick and Goldstein,¹⁸ in which some definite mendelian mechanism is assigned to otosclerosis. Guild,¹⁹ however, in his studies of histologic otosclerosis, stated facts that he considered to "render invalid all conclusions, with respect to dominant and recessive genes, that have been drawn from clinical studies of the inheritance of otosclerosis." This opinion has been expressed by others.^{1, 20} It is therefore impossible to prophesy deafness of progeny⁹ and it would be futile to try to eliminate otosclerosis by eugenic measures,^{11, 19} such as preventing propagation by otosclerotic subjects, as suggested by Guggenheim.²¹

SUMMARY AND CONCLUSIONS

Otosclerosis is a pathologic process of unknown etiology wherein new spongy bone is formed about the stapes and oval window, resulting in progressive deafness. This process is frequently unfavorably affected by pregnancy, as well as by other endocrine crises. The loss of auditory function may occur at any time in relation to pregnancy — during or after it or six months or so after parturition.

In this series, 72 per cent of the patients suffered hearing loss with the first pregnancy and 50 per cent with subsequent ones. The effect of abortion, like the effect of pregnancy, on the otosclerotic process is entirely unpredictable in the single case.

Abortion is never justified in the management of otosclerosis, for three reasons. First, the effect of pregnancy on otosclerosis is extremely variable and unpredictable, and there is no exact relation between the two conditions. The effect of previous pregnancies is not an accurate index of the effect of subsequent ones. Second, the favorable effect of abortion on the otosclerosis is also inconstant. The progression of the deafness with pregnancy may or may not be arrested by abortion. Third, the disease does not endanger the life of the mother,

as do the accepted indications for therapeutic abortion, such as tuberculosis, heart disease and toxemia. Fourth, this type of deafness is not the severe handicap that it once was, owing to the advent of the modern hearing aid and the promise of surgical treatment.

Sterilization or other eugenic measures are futile in the control of otosclerosis, because the hereditary nature of the disease is not known accurately and it is impossible to prophesy deafness of progeny, and because the unfavorable effect of pregnancy on otosclerosis is not constant. In this series, the patients had a 50 per cent chance of having successive pregnancies without damage to the hearing. The final decision concerning the role of abortion and sterilization in otosclerosis rests on a complete understanding of the etiology of the disease.

I am indebted to Dr. George Kelemen for the translation of the German articles.

243 Charles Street

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MEDICAL PROGRESS

INDUSTRIAL HYGIENE

IRVING R. TABERSHAW, M.D.*

BIRMINGHAM, ALABAMA

ALTHOUGH the stimulus of war is no longer spurring the growth of industrial hygiene, many of the advances made during the world conflict will continue to develop. Some of the problems behind this country's industrial achievements have been brought into focus. One of these is the question of safe and healthful working conditions, and both labor and management have been fully awakened to industrial health as a factor in collective bargaining. It is to be expected that industrial medicine in the future will play a more active part in such questions. The excellent work of governmental agencies in aiding the solution of industrial-health problems is recognized by the continued growth of these organizations.¹ During the war they operated under restrictions of personnel and material, both of which are now being corrected. Undoubtedly there will be a further increase in governmental industrial-hygiene activities after peacetime reconversion is completed. At present there are forty-four official state, county and city industrial-hygiene units.

Another development in this last year of war has been the crystallization in the minds of physicians of the concept that industrial medicine is an essential part of modern practice. They are realizing the importance of industrial medicine in helping the United States to maintain its position as the most powerful industrial nation in the world. Many physicians have signified their interest in working with industry. This has been brought out by a questionnaire to Army and Navy medical personnel in which over 20 per cent of those answering indicated that they were interested in some phase of industrial medical practice.² To take care of the need of postgraduate courses nine universities are now prepared to supply advanced training in industrial health.³

Rehabilitation of the veteran continues to be one of the major post-war problems. Discharged men with physical handicaps are being competently guided back into useful life. The problem of the psychoneurotic, which is as great as that of veterans with a physical handicap, is not being overlooked.⁴ The concern of American medicine with the economics of medical practice is evidenced by the number of reports on various industrial-health plans.⁵⁻⁹ The features of each plan usually develop

as a result of local conditions, and the further growth of medical care through the medium of industry is to be expected. During the past year tuberculosis surveys were actively promoted among industrial workers by federal and state agencies.

PNEUMOCONIOSIS

Radon has been implicated as the agent responsible for the high incidence of lung cancer in the Schneeberg and Joachimsthal mines, where it caused fifty per cent of all deaths of miners. Among contributory factors mentioned as possible etiologic agents in this mining region are dust, chronic respiratory disease, arsenic and perhaps hereditary susceptibility. A recent review of the factors by Lorenz¹⁰ casts doubt that radium or radon has ever induced lung cancer in man. Animal experimentation and studies of other industrial workers exposed to radon do not substantiate the opinion that radioactivity produces lung cancer.

The acute toxic effects produced by quartz have been ascribed by one group of investigators to soluble silica. Others¹¹ have been unable to demonstrate that soluble silica is toxic, but find that the action of body fluids liberates irritating colloidal silica on the surface of quartz particles. Confirmatory evidence that colloidal silica produces toxic effects in the lungs has been furnished by perfusing lungs with this material, a specific pharmacologic bronchoconstrictor effect being thus demonstrated. Particulate silica and silica in soluble form produced no response under the same conditions. The evidence suggests that on contact with body fluids the surface of finely divided quartz may be converted to highly active colloidal silica.

Objective satisfactory tests for study of the disability arising from silicosis or other pneumoconioses have not been devised, but physiologic and clinical study provide some useful data. In a study of two groups of patients, one with silicosis and the other with siderosis, Enzer et al.¹² found that both groups showed depression of functions compared with the normal limits. This was much more marked in the latter group than in the former. The silicotic patients, however, were, on the average, thirteen years older than those with benign pneumoconiosis which may account for the difference in physiologic response. It is significant that a depression of normal functions was found in a group of subjects suffering from so-called "benign

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pneumoconiosis." The difficulties inherent in determining disability in those suffering from pneumoconiosis is ably described by Wright.¹³ Further investigative work on this problem is needed.

So-called "eggshell" calcifications have been reported in the chest films of silicotic patients, especially slate quartz miners. There is no unanimity of opinion concerning the cause of these calcified areas or even their roentgenographic distribution since some investigators maintain that they occur only in the mediastinal lymph nodes, whereas others describe them as extending into the lung parenchyma. Riemer¹⁴ reports 4 cases occurring in workers who besides being exposed to silica dust were also exposed to limestone. He suggests that these calcifications may have been due to the inhalation of calcium.

Three acute cases of chemical pneumonitis due to exposure to beryllium were reported by Van Ordstrand et al.¹⁵ in 1943. This metal has been identified as the causative agent in the production of a chronic pneumonitis characterized by dyspnea, orthopnea and miliary nodulation as disclosed by x-ray study and autopsy. A series of such cases occurred in Massachusetts, and confirmatory evidence is accumulating in other sections of the country where beryllium is used. Beryllium and its compounds are of increasing importance in present-day electronic manufacture and atomic research, and investigations are being conducted in an attempt to correlate acute and chronic manifestations of diseases induced by this substance.

The problem of benign pneumoconiosis has been reviewed by Pendergrass and Leopold,¹⁶ who point out that it is impossible to differentiate the roentgen-ray appearance of silicosis or benign pneumoconiosis from that of many pulmonary diseases unassociated with the inhalation of dust. The diagnosis of such pulmonary lesions depends on a detailed knowledge of the occupational history and the environmental conditions of the worker, especially as regards the nature, concentration and particle size of the dust to which he has been exposed. The incidence of nodulation in the lung parenchyma is increasing owing to the development of manufacturing techniques in which iron and other dusts are generated, for example, welding and metal grinding.

The widespread taking of x-ray photographs in industry has demonstrated numbers of people, chiefly farmers, with pulmonary miliary calcifications that apparently produce no symptoms.¹⁷ These nodules usually consist of discrete, dense, round, uniform, shotlike spots scattered over the lungs. The causative agent has long been considered to be the tubercle bacillus, but there is some possibility that *Aspergillus* is the cause. *Histoplasma capsulatum* has also recently been suggested as a cause of pulmonary calcifications in the tuberculin-negative subject.¹⁸ No data are available on the

significance of these findings in relation to industrial exposure to dust.

Ritter and Nussbaum,^{19, 20} in reviewing occupational illness in the cotton industry in Mississippi, state that they have been unable to find any evidence that byssinosis exists as a clinical entity. An acute febrile disease of short duration, known as "cotton fever," almost universally develops among workers when first exposed to high concentrations of cotton dust or when they return to such exposures after periods of absence. There is no evidence that chronic changes follow these manifestations. Allergic workers may develop hypersensitivity to cotton dust.

Attention has been called to a type of pneumoconiosis produced in boiler scalers, who are exposed to dust consisting of silicates, iron and salts of sodium, magnesium and calcium. The abnormal shadows seen in the x-ray films of these workers are said to be due partly to silicotic-fibrosis and partly to deposits of iron dust.²¹

ALUMINUM THERAPY AND PROPHYLAXIS IN SILICOSIS

Powdered metallic aluminum and amorphous hydrated alumina (XH.1010) have both proved valuable in preventing silicosis in animal experimentation. Corroboration of the effectiveness of neutralizing the toxic effects of silica is evidenced by the improvement in disabled silicotic patients when treated by inhalations of either of these compounds. An organization (McIntyre Research Limited, Toronto, Canada) has been founded by the original experimenters with aluminum to develop research in silicosis control, hence, to use aluminum in this manner, a license must be obtained through this company.

There is no confirmation of the pneumoconiosis described in recent years by German investigators as being caused by the inhalation of aluminum dust. Another study of pulmonary findings in workers exposed to heavy concentrations of aluminum oxide indicated no evidence of pulmonary fibrosis.² It must be kept in mind that the exposure of industrial workers to aluminum is not the same as that when it is used therapeutically. In industry, factors such as the specific compound, particle size and degree of concentration must be ascertained to compare toxicities.

A number of investigators have substantiated the favorable clinical results obtained by Hannon² on silicotic patients in the ceramic and foundry industries. In treating small groups of miners Gardner²⁴ did not obtain the same startling improvement, although some of his patients showed subjective improvement. Bamberger²⁵ in treating a group of miners obtained subjective improvement in about 50 per cent of the cases. He used both powdered metallic aluminum and hydrated alumina, and states that the latter is preferable since it is

white color is less objectionable and since it appears to be more stable, does not require a bulky mill to produce it and seems to be less irritating to the respiratory tract, as evidenced by the fact that it causes less discomfort on inhalation. There is a wider experience with the use of powdered metallic aluminum, however, and it appears that the choice of either agent is a matter of personal preference.

Objective evidence of improvement in silicotic patients treated with aluminum is difficult to demonstrate, and the mechanism by which aluminum is rendered effective is not clearly understood. It is said to relieve bronchospasm, which is responsible for some of the pulmonary dysfunction. Gaseous exchange in the lungs may be interfered with by the inflammatory and immature fibrotic changes that thicken the alveolar walls of silicotic patients. Since aluminum causes regressive changes, some improvement may be due to this phenomenon. These regressive changes have not been demonstrated by x-ray.

All the data on the efficacy of aluminum as a prophylactic agent have been obtained through animal experimentation. To determine its efficacy in human beings will require many years, since silicosis does not appear on the average until ten years of exposure to a harmful concentration of the silica dust have elapsed. Engineering control should still be the recommended method for the prevention of silicosis, since dust control has the advantage of providing a cleaner work place, decreasing the psychologic hazard in the worker's mind of constant exposure to dust and diminishing the burden of the protective mechanism of the lungs in handling extraneous inhaled material. It therefore appears that at this time aluminum as a prophylactic agent should be considered only as an adjuvant to engineering control. There is no doubt that the therapeutic use of aluminum is worthy of extensive clinical application, and in several score of industrial plants aluminum is now being administered on that basis.

INDUSTRIAL POISONS

So many chemicals are used in industry that it is possible to review only a fraction of those whose toxicity has been studied. It is noteworthy that lead poisoning and benzol intoxication have decreased, this being reflected in the paucity of published articles on these two substances, which were for so long pre-eminent in industrial hygiene. The decrease in lead poisoning is emphasized by Hoffman,²⁶ who shows a steady decline in the number of cases from 1916 to 1942. This improvement is undoubtedly due to the progress made in industrial-hygiene methods regarding protective engineering devices and regular medical examinations of workers, since the use of lead in industry has increased considerably. Occasional cases of aplastic anemia due to benzol are still reported.²⁷

One of the unsolved problems in preventive industrial medicine is the development of methods to determine the early deleterious effects of exposure to chemicals. An advance in the direction of determining the early effects of hepatotoxic compounds has been made. A simple test for the determination of bilirubin in the urine consists of adding five drops of 0.2 per cent aqueous methylene blue to 5 cc of urine. If bilirubin is present, a green color is produced. This test is still experimental but has already shown its worth in the diagnosis of preicteric hepatitis.²⁹ Myers²⁹ has used it in workers exposed to tetrachlorethane and has proved its usefulness in protecting employees from further exposures to these toxic fumes.

Carbon monoxide still continues to be the most frequent cause of fatal industrial poisoning. Repeated exposure to small doses apparently induces no chronic effects. The most serious sequelae are neurologic, owing to degeneration of the brain, but occur in only a small percentage of cases following extreme exposure. The most characteristic lesion is in the lenticular nucleus, especially the globus pallidus. Experimental chronic carbon monoxide poisoning in dogs has shown that cardiac changes closely resembling those due to anoxia from other causes are produced. These changes are demonstrated by electrocardiographic variations and by morphologic changes, which include degeneration, hemorrhage and necrosis in cardiac muscle fibers. It was noted that chronic carbon monoxide intoxication in dogs occurred in concentrations that have been regarded as being within the safety limit for man.^{30, 31}

Ethylene chlorhydrin, a compound frequently used in chemical synthesis and as a solvent, has been responsible for several deaths.^{32, 33} The chief pathological findings were in the liver, lungs and kidney. Experimental work confirms its toxicity and the fact that it may cause death by absorption through the skin.³⁴ It is estimated that the lethal dose of ethylene chlorhydrin on the skin may be less than 5 cc. In all processes using this material human contact must be avoided, since there are no effective protective measures.

As the results of experiments during World War I, preventive measures were instituted at the very beginning of World War II in all plants manufacturing explosive powders. In spite of this early and planned precautionary program and a great deal of experimental research,³⁵ exposure to trinitrotoluene still produces occasional fatalities. Eddy^{36, 37} describes 3 cases of aplastic anemia in workers exposed to only 1.5 mg of trinitrotoluene per cubic meter of air, the accepted maximum allowable limit. During the course of the disease the patients exhibited anemia and neutropenia, and the most important symptoms were weakness, sore mouth, purpura and respiratory complaints. There is apparently an individual susceptibility.

Reactions other than those due to aplastic anemia are hepatitis, dermatosis and gastric complaints

Methyl bromide has been finding an increasing use as a refrigerant, fumigant and insecticide. Chronic exposure to concentrations of less than 35 parts per million may cause gastrointestinal symptoms, headache and diplopia, and higher concentrations may lead to coma and convulsions.³⁸ On the skin it produces characteristic vesicular burns. Johnstone³⁹ describes an outbreak of methylene bromide intoxication in 20 packers exposed while fumigating dates. The symptomatology was chiefly referable to the central nervous system, with production of visual disturbances, ataxia, numbness of the extremities, apathy, somnolence, hallucinations, melancholia, coma, convulsions and maniacal states. In all cases there were some speech difficulty, visual disturbances and ataxia. Apparently no permanent disability resulted from these exposures.

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PHYSICAL HAZARDS

Environmental conditions of heat and humidity in certain industries may be severer than those occurring in natural climates. The question of which temperatures cause only discomfort and inefficiency at work and which actually cause damage to health is complicated by factors of individual acclimatization and by the lack of an adequate system of correlating various combinations of temperature, humidity and air motion. All investigators of these problems agree that the wet-bulb temperature is the limiting factor in man's ability to tolerate hot environments. An exhaustive study by Eichna and his colleagues⁴⁶ determined the upper limits of environmental heat and humidity tolerated by acclimatized men in good physical condition working in hot environments. Healthy, acclimatized men work easily and efficiently when the wet-bulb temperature does not exceed 91°F. Between 91 and 94°F they work with difficulty and inefficiently and mild heat casualties may occur. At a wet-bulb temperature of 94°F they are in-

capable of sustained effort and a high incidence of heat casualties is to be expected. Dry-bulb temperatures below 120°F have no appreciable effect.

Skinner and Pierce,⁴⁷ in evaluating environmental conditions of heat and humidity in Massachusetts, used an effective temperature of 86°F as the maximum allowable for comfort and efficiency at work. Engineering methods are available to combat the production of high temperatures in industry, and medical methods help to control deleterious effects. Ten methods of overcoming these conditions, together with an analysis of common mistakes in engineering practice for controlling heat and humidity, are reviewed in this article. A number of experiments on the effect of vitamin depletion through sweating have been performed. Mills⁴⁸ found in studying acclimatization to tropical heat that men showed a need for almost double the dietary thiamine per unit of food and a manyfold increase in choline, which under such conditions becomes a nutritional factor of great importance. Other investigators,^{49, 50} who used vitamins B₁ and C as supplementary dietary factors in workers exposed to high conditions of temperature and humidity, state that no benefit is derived from the additional intake of vitamins. The use of salt, in tablets or by salting the drinking water, to replace the chloride lost in the sweat is still basic in the treatment of physiologic disturbances from heat exposure.⁵¹ The administration of glucose is of no advantage. Workers in hot environments maintain better efficiency if the water loss is replaced hour by hour.

Audiometric studies of workers exposed to loud noises have indicated that there may be permanent impairment of hearing. There is an awakening to this danger, although for a long time evidence has been available that fatigue, irritability, anorexia and decreased efficiency at work may be ascribed to loud noises. Engineering methods to reduce the production of noise are still inadequate, and protection must be obtained by personal protective devices.⁵² Special earplugs have been developed for this purpose, although the use of cotton alone is usually sufficient to reduce the noise by five to ten decibels. This simple method frequently prevents the harmful effects of excess of noise.

RADIOACTIVE SUBSTANCES

Interest in the health hazards caused by uranium has been awakened by the development of the atomic bomb. The alpha particle radioactivity of this substance has been utilized to follow its course in the body.⁵³ From 31 to 88 per cent is eliminated in the urine in the first twenty-four hours after intravenous injection of uranium nitrate in dogs. It was found that the administration of large doses of sodium citrate facilitated the excretion of uranium.^{54, 55} This therapeutic measure was successful in causing survival in dogs receiving an otherwise

lethal dose The effect of sodium citrate in reducing the toxic action of uranium is not completely understood, but it is suggested that its alkalinizing effect does not permit development of the acid reaction necessary for precipitation and necrosis of renal protein Further developments may be expected in the field of health hazards in atomic research, since the work occasions exposure to radioactivity in beryllium and other less known elements

It is to be expected that chronic radium poisoning will be frequent in the next few years, since many thousands of workers were exposed because of expansion of the luminous-dial-painting industry during the war Unfortunately, preventive measures were not universally applied, but in cases in which environmental studies were coupled with radon determinations of expired air of workers, no deleterious effects are expected Evans, Harris and Bunker⁵⁵ produced chronic radium poisoning in rats by oral administration Hypercalcification, bone fragility and, at the end of a year, a high incidence of osteogenic sarcoma were produced Rats were found to be more tolerant of the radium than was man Quantitative study showed that 4 to 8 per cent of the ingested radium is retained, and that on death an average of 3 per cent remains, over 90 per cent of this being retained in the skeleton

DERMATITIS

Although industrial dermatitis is recognized to be the most frequent disease of occupational origin, exact data on its incidence and causative factors are not available In most states, occupational disease is not reportable, and in many of the states in which these conditions must be reported serious inadequacies exist The most comprehensive data on the number and types of dermatitis cases in industry are presented by Brinton and Schwartz,⁵⁷ who have analyzed 32,512 cases reported by seven states for the five-year period 1938-1942 It has been observed that in certain industries the principal dermatitis-producing agent is similar to the manufactured product—notably in the manufacture of explosives, plastics, rubber, food products and leather Industries engaged in the manufacture of metals show oils and greases to be the principal etiologic agent for dermatitis In nearly half the industrial groups exposure to no single material existed The dermatitis-producing agents are classified under twenty-seven headings The most frequent causes of skin disease are petroleum products and greases (18.8 per cent), alkalis (11.7 per cent), solvents (7.8 per cent), plants and woods (6.5 per cent) and metals and metal plating (6 per cent) It is to be hoped that more accurate data will be developed as additional states require the reporting of occupational diseases and that the deficiencies of present methods will be corrected

The allergic reactions of the skin are foremost in the interest of industrial dermatologists, since much

of the skin disease in industry is due to sensitizing agents A phenomenon that has been repeatedly observed clinically is so-called "hardening"—that is, the disappearance of an allergic contact-type dermatitis in sensitized persons on repeated exposure to the sensitizing chemical while they are still at work⁵⁸ This finding has made it possible to continue the employment of sensitized subjects in industry and has been especially noted in workers exposed to tetra-*n*-butyl phenolformaldehyde and other allergens It should be noted that hardening does not occur in all persons, that in most cases it disappears if exposure to the sensitizing chemical is discontinued, and that exposure to a great concentration of the sensitizing substance may cause recurrence of the dermatitis One investigator questions the occurrence of this phenomenon, contending that persons showing a low degree of hypersensitiveness may continue to work under conditions of minimal exposure

The exact place of the patch test in the diagnosis and treatment of occupational dermatitis is still subject to some controversy⁵⁹ ⁶⁰ Most authorities agree that the preplacement patch test is not a diagnostic procedure suitable to industry In all cases in which patch tests are employed the tester must be fully familiar with all factors necessary to obtain a result capable of interpretation Dermato-phytosis and its allergic manifestations are not an important factor in lost time in industry, in spite of the wide prevalence of this disease There is no indication that the presence of an allergy to a fungus in a worker bears any relation to the acquisition of an allergic contact dermatitis⁶¹

Investigations of outbreaks of occupational dermatitis in industry continue to add to the list of industrial substances known to be primary skin irritants or sensitizers Many of these are of great importance in war industries, especially in regard to explosives⁶² On the other hand, cutting oils, fabrics, synthetic rubber and plastics, which account for so many cases, are even more widely used in a peacetime economy The manufacture of food products has been investigated, since contact dermatitis is the most frequent cause of occupational illness in this industry⁶³ The dermatitis of fishermen, which in some cases is unique, and erysipeloid and "redfeed," which are confined almost exclusively to fishermen, have been described⁶⁴

MISCELLANEOUS CONDITIONS

Advances continue to be made in methods for the detection and quantitative determination of chemical industrial poisons The use of the polarograph has proved of special merit, since it has the advantages of speed, precision, uniformity, relative freedom from interferences and the possibility of simultaneously determining two or more substances Levine⁶⁵ has outlined the procedures for the determination by polarographic means of atmospheric

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor**

BENJAMIN CASTLEMAN, M D, *Acting Editor*

EDITH F PARRIS, *Assistant Editor*

CASE 31411

PRESENTATION OF CASE

A seventy-seven-year-old woman was admitted to the hospital in a semicomatose condition. The history was obtained from relatives.

Two days before admission, in the morning, the patient became nauseated and vomited a considerable quantity of greenish fluid. She later complained of severe intermittent pain throughout the abdomen and in the back. On the day before admission there was no nausea or vomiting. She drank about 3 quarts of water but did not urinate all day. A bowel movement was obtained only by an enema. She was seen by a physician, who found the white-cell count to be 15,500. Later that day she became semi-stuporous. On the day of admission she passed by rectum a large amount of foul-smelling gas. In the morning the temperature was 100°F, and the pulse 120, she was admitted in the afternoon.

Her blood pressure in the past had averaged 150 systolic, 90 diastolic. For many years fatty foods had resulted in gas and mild abdominal pain. Because of her abdominal complaints, she had had numerous x-ray studies at other hospitals over the past ten years. Two diverticula of the esophagus were found, and there were numerous diverticula in the colon, particularly in the sigmoid. A Graham test the previous winter had revealed no stones in the gall bladder. She had had occasional episodes of mild diarrhea alternating with constipation. A number of years before admission a diagnosis of

*On leave of absence

pyelitis was made, but recently the patient had complained of no dysuria, pyuria or hematuria. There had been no vaginal bleeding or discharge since the menopause.

On examination the patient was in a semiconscious state, with moderate respiratory distress. The skin was cold and clammy. The pupils were pinpoint. The lips and tongue were dry, and the former blue. The heart sounds were distant. A systolic murmur was heard at the apex and base. The pulse was weak. The lungs were clear. The abdomen was moderately distended and diffusely tender. There was tenderness in both costovertebral angles. No fluid wave was elicited, and peristalsis was normal.

The temperature was 102°F, the pulse 130, and the respirations 30. The blood pressure was 90 systolic, 45 diastolic.

Examination of the blood revealed a white-cell count of 25,000. The hemoglobin (Sahli) was 9.0 gm per 100 cc. No urine could be obtained by catheter.

The patient continued in coma. The respirations were rapid, shallow and labored. The blood pressure remained at 90 systolic, 50 diastolic. An intravenous injection of 5 per cent dextrose in water was given with great difficulty because of collapsed veins and the fact that the patient resisted bitterly when venous puncture was attempted, indeed, the needle was placed only after she had received 4 cc. of paraldehyde intramuscularly. A whole-blood transfusion of 500 cc was given on the evening of admission. The respirations became slower, and the patient expired fifteen hours after admission.

DIFFERENTIAL DIAGNOSIS

DR FRANCIS D MOORE. This is the story of a seventy-seven-year-old patient who came into the hospital in shock, and who died about sixty-three hours after the beginning of her illness. That length of elapsed time is significant, because diseases that kill people in forty-eight hours or less are often events having to do with the cardiovascular system, such as cerebral accidents, aneurysms, coronary occlusions and so on. This patient did stay alive long enough to die of one of the intra-abdominal

concentrations of lead, zinc oxide, cadmium, chromic acid and manganese

The preventive program instituted at plants engaged in making phosphorus has eliminated the appearance of the characteristic so-called "phossy jaw," which was so frequent during World War I. It is now recognized that the earliest sign of the development of a lesion due to phosphorus is osteoporosis of the maxilla or mandible, which can be determined radiologically but is no different from that of any osteomyelitis of dental origin. Dental hygiene is extremely important, and workers who have dental extractions should be kept away from phosphorus for a period of four to six weeks to allow complete closure of the socket.^{66, 67}

Leptospirosis may be considered an occupational disease, since workers exposed to water infected with rat urine show an overwhelming incidence of the disease. Thirty-seven cases were reported in Hawaii in cane cutters,⁶⁸ and in a mine in Alabama 27 cases occurred in a period of seven years. Sporadic cases in food handlers, fishermen and so forth continue to be reported in the literature. The disease is apparently amenable to treatment with penicillin if large enough doses are given. Many cases are still undiagnosed until autopsy.

* * *

The first year after the war should bring many interesting changes in industrial hygiene. A number of hazards that have been kept military secrets, such as those associated with atomic research, radar and so forth, should come to the fore. Industrial development in plastics and electronics will provide medical investigators with an opportunity to see many more cases of occupational poisoning. Some of the less tangible benefits of industrial hygiene will prove themselves to be more important as labor and management arbitrate grievances arising out of health conditions in industry.

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ANATOMICAL DIAGNOSES

Acute hemorrhagic pancreatitis with widespread fat necrosis

Thrombosis of splenic, inferior mesenteric and portal veins

Gangrene of descending colon, sigmoid and rectum

PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMAN The autopsy on this patient showed about 500 cc of thin, hemorrhagic fluid in the peritoneal cavity. There was no evidence of peritonitis, but we got the clue to the diagnosis when we saw multiple foci of fat necrosis throughout the upper abdomen. There was an extensive hemorrhagic pancreatitis, with severe necrosis of the entire body and tail. The head of the pancreas was relatively free from hemorrhage. As is almost the rule, the necrotizing process had involved radicles of the splenic vein, and in this case there was thrombosis of the main splenic vein, with retrograde extension involving the inferior mesenteric vein, so that as a complication of the pancreatitis there was venous infarction of the descending colon, sigmoid and rectum. It was the first case that I had ever seen with this type of complication, although I am sure that it must occasionally occur. The thrombosis also extended down to the mouth of the portal vein but entered it only for a short distance and had not occluded it. There was no involvement of the superior mesenteric vein, so that there was no disturbance of the blood supply to the right side of the colon. The stomach and duodenum were markedly hemorrhagic. Do you know, Dr Donaldson, what happened the evening before the attack? Had she had a heavy meal or had she taken quite a bit of alcohol?

DR DONALDSON I am sure that she had not.

DR CASTLEMAN A heavy meal might have caused the duodenitis. The papilla of Vater was markedly edematous, and although we did not find complete obstruction at autopsy, at one time it might have been constricted enough to have caused the pancreatitis.

DR MOORE Did you find any other disease of the biliary tract?

DR CASTLEMAN She had a so-called "strawberry gall bladder," but there were no stones and there was free flow of bile through the common duct into the papilla at the time of autopsy. This bile was forced through by pressure on the gall bladder and, as Rich* has pointed out, this is a post-mortem procedure that may not represent the state of affairs in vivo. There was nothing significant about the kidneys, and the anuria was probably due to shock.

A PHYSICIAN How valuable is the symptomatology? The history states that for years she had been troubled with gas and abdominal pain. Is

there any connection between that and the pancreatitis?

DR CASTLEMAN She had cholesterosis of the gall bladder. Whether that produces symptoms at times I do not know. At the time of autopsy the gall bladder was markedly distended, so that there probably was obstruction at the papilla at one time.

DR MOORE That can follow pancreatitis as well as cause it. It is not infrequent.

CASE 31412

PRESENTATION OF CASE

First admission. A sixty-five-year-old machinist was admitted to the Emergency Ward complaining of chest pain.

The patient had had a cold and cough for several weeks. Three days before admission, while changing position in bed, he was suddenly seized by pain in the anterolateral part of the right lower chest, which was relieved by lying on his right side. There were no chills or fever, and the cough remained unchanged.

For eight years before admission, whenever he walked hurriedly, he had noted a dull aching pain starting in the left wrist and radiating upward across the shoulders and down the right arm. Nitroglycerin relieved the pain in a short time. Palpitation occurred infrequently. There had been no ankle edema at any time.

Physical examination revealed a short, stocky man in some respiratory distress. The throat was slightly injected. There was dullness to percussion over the right lung base anteriorly and posteriorly, with decreased breath sounds and moist rales. The respiratory excursions of the right chest were limited. There were moist rales at the left base, but no dullness. The heart sounds were distant. The rate was regular, and no murmurs were audible. The cardiac outline was indistinct to percussion.

The temperature was 98.4°F, the pulse 80, and the respirations 24. The blood pressure was 150 systolic, 90 diastolic.

Examination of the blood showed a white-cell count of 7800. The urine was normal.

An x-ray film of the chest taken the day before admission showed the diaphragm to be smooth in outline, with normal motion. The heart was slightly prominent in the region of the left ventricle. The aorta was tortuous. There was no definite evidence of consolidation in the lungs. A throat culture revealed a few beta-hemolytic streptococci. An electrocardiogram revealed normal rhythm, with a rate of 70, a PR interval of 0.14 second, slight depression of ST₁, inverted T₁, upright T₂ and T₃, deep, late inversion of T₄, and left-axis deviation.

The patient was discharged improved on the second hospital day.

*Rich A. R., and Duff G. L. Experimental and pathological studies on pathogenesis of acute haemorrhagic pancreatitis. *Bull Johns Hopkins Hosp* 58:212-259, 1936.

catàstrophes that may be treated by the surgeon. That does not rule out the other causes of reasonably sudden demise, but it does make it necessary to include consideration of peritonitis and its various causative factors.

We need not labor the question whether this patient was in shock. The blood pressure was 90 systolic, 50 diastolic, having previously been 150 systolic, 90 diastolic, and it stayed that way. She was anuric, the veins were collapsed, the pulse was weak, the heart sounds were distant and she was slightly cyanotic, it is fair to say that she was in shock.

What else did she have when she came in? She had a moderately distended and diffusely tender abdomen, which entitles one to say that she had peritonitis. A peritoneal cavity filled with blood could give that picture, but if she had had a massive intraperitoneal hemorrhage I should not have expected her to live this long. So I think that she had peritonitis and shock resulting from the peritonitis and that she died therefrom. The problem is, therefore, to find out why she had peritonitis and to see if there are any clues in the past history that might help us.

A perforated gall bladder with bile peritonitis certainly can occur in this age group, but from the evidence we have it is unlikely. A Graham test, presumably done several months before, had shown no stones in the gall bladder, and we have to accept that at its face value. There were numerous large-bowel diverticula, particularly in the sigmoid, and she occasionally had episodes of mild diarrhea alternating with constipation. So I think that it is fair to say that she had diverticulosis, with alterations in large-bowel motility and occasional mild inflammation.

Can diverticula in the large bowel produce the symptoms with which this woman died? Diverticula of the sigmoid may become inflamed and perforate and cause generalized peritonitis with great rapidity. Perforated diverticula of the sigmoid may follow other paths. After prolonged inflammation they may perforate locally and form small pericolic abscesses. These abscesses may later heal, the resulting sclerosis producing a picture of sigmoidal obstruction that is difficult to differentiate from that due to carcinoma. This patient had nothing to suggest that type of diverticulitis, and if we were to blame the final illness on diverticulitis, we should have to say that she had an open perforation into the peritoneal cavity, with no previous walling off, and massive fecal peritonitis.

There are, of course, many other things that can cause a massive peritonitis that is fatal in this short period of time. Perforation of the bowel by a foreign body, including swallowed objects, has caused rapidly fatal peritonitis. Internal hernia or other lesions involving loss of blood supply

to the bowel can produce fatal peritonitis, but usually not in sixty-three hours. A perforating carcinoma of the sigmoid or an ulcer of the stomach can cause fatal peritonitis, but the latter rarely occurs in a seventy-seven-year-old woman. Such a diagnosis would have to be just a guess in this patient, as there is no evidence in the record to provide a background for a lesion of this type. Furthermore, the story is not suggestive of appendicitis.

There is one other line of evidence that I ought to dispose of, namely, the costovertebral angle tenderness. The patient was anuric and had pain in the back. Back pain, of course, can be caused by any intra-abdominal inflammatory process that involves the retroperitoneal tissues. The facts that she was anuric and that she had costovertebral tenderness are disturbing because they suggest that she had urinary obstruction and that this was somehow responsible for the apparent anuria. But on the evidence that we have I do not believe that we ought to take that too seriously. She was in severe shock with the peritoneal lesion, and the loss of body fluid into the peritoneum did not leave enough for the kidneys to excrete.

So my diagnosis is a perforated diverticulum of the large bowel, presumably of the sigmoid, although the record states that they were scattered throughout the large bowel and a cecal diverticulum can at times perforate and cause peritonitis.

DR. FREIDRICH KLEMPERER: Would you expect peristalsis to be normal in this condition?

DR. MOORE: No.

DR. KLEMPERER: It is said to have been normal.

DR. MOORE: That is correct.

A PHYSICIAN: How about pancreatitis?

DR. GORDON DONALDSON: I should like to point out the fact that this patient did have normal peristalsis when I saw her at home, and also when she came into the hospital. There was some question whether she ought to be brought to the hospital, because there was evidence of early peritonitis at home, and by the time she came in here it had spread. The trip certainly threw her into shock. All I can say is that we thought she had peritonitis and that all our efforts were directed in trying to bring her out of shock. There was never any question of operation. We spent several hours trying to give intravenous injections, and we finally succeeded in giving a transfusion. That is all we could do.

CLINICAL DIAGNOSIS

Peritonitis

DR. MOORE'S DIAGNOSIS

Perforated sigmoidal diverticulum, with peritonitis, shock and resultant anuria

ANATOMICAL DIAGNOSES

Acute hemorrhagic pancreatitis with widespread fat necrosis
Thrombosis of splenic inferior mesenteric and portal veins
Gangrene of descending colon, sigmoid and rectum

PATHOLOGICAL DISCUSSION

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CLINICAL DIAGNOSIS

Peritonitis

DR. MOORE'S DIAGNOSIS

Perforated sigmoidal diverticulum, with peritonitis, shock and resultant anuria

which he succumbed as a result of his already damaged heart. There is, however, only a little evidence in favor of an abdominal emergency. The location of pain is certainly abdominal. He vomited, and there was some blood in the vomitus. He had normal peristalsis on admission, and a few hours later it was absent. There was tenderness in the abdomen. One thinks of any of the acute abdominal emergencies and could make a long list of possible diagnoses, but there is no good evidence to support any of them. I have written down ruptured viscus, acute hemorrhage, acute pancreatitis and thrombosis of some abdominal vessel. But against these diagnoses is the fact that the signs in the abdomen were not particularly definite. I should not be surprised to learn that any patient may have absent peristalsis in the last hour or two of life.

The friction rub is significant. If there actually was a friction rub, it would be hard to explain this patient's death on the basis of an abdominal catastrophe. Occasionally adventitious sounds are heard in the chest that are mistakenly diagnosed as a friction rub, but I do not believe that we have the right to suggest that in this case. If he had a friction rub, the lesion must have been in the chest. Therefore, my diagnosis is myocardial infarction. I do not know whether it was an early one, with shock and failure rapidly precipitating death, or whether it was some two or three weeks old, with a fatal complication, such as a ruptured ventricle.

CLINICAL DIAGNOSIS

Coronary thrombosis, with myocardial infarction

DR HARWOOD'S DIAGNOSIS

Myocardial infarction

ANATOMICAL DIAGNOSES

- Acute hemorrhagic pancreatitis
- Coronary sclerosis
- Myocardial fibrosis

PATHOLOGICAL DISCUSSION

DR CASTLEMAN The clinical diagnosis was the same as that of Dr Harwood. In fact when this patient was brought into the Emergency Ward the medical resident pointed him out and said without knowing anything about the case, "He looks like a patient with a myocardial infarct."

At autopsy the heart weighed 450 gm, with hypertrophy predominantly of the left ventricle. In the anterior wall there was diffuse myocardial fibrosis that might be called a healed infarct. The coronary arteries were sclerotic, but there was no evidence of acute thrombosis or acute myocardial infarction.

Here again, the diagnosis was an acute hemorrhagic pancreatitis. This was much severer than that in the preceding case, involving the entire pancreas. There was no evidence of gall-bladder disease. We traced the pancreatic duct from the tail into the neck, and then it was lost. We could not find any communication between the pancreatic duct and the ampulla. The main splenic artery and veins were normal. There was some extension of the hemorrhage into the peritoneal cavity, but not so much as there was in the preceding case.

DR HARWOOD How do you explain the pericardial friction rub?

DR CASTLEMAN I do not know. Several examiners heard it, and they even charted just where in the course of the beats it occurred. It was believed to be a pleuropericardial friction rub.

DR OLIVER COPE The heart was large. Might that have accounted for it in any way?

DR CASTLEMAN Dr Jones, what about that?

DR T DUCKETT JONES I do not believe so.

DR MOORE What was in the peritoneal cavity? Bloody fluid?

DR CASTLEMAN A small amount.

DR MOORE Was there fat necrosis?

DR CASTLEMAN Around the pancreas and over a few areas near the lesser sac. The lesser sac contained a fair amount of blood.

Final admission (seventeen months later) About eighteen hours before entry the patient began to perspire profusely, and twelve hours later was seized with severe, subxiphoid pain. A physician gave him a hypodermic and sent him to the hospital.

The patient was in a shock-like condition on admission. The skin was cool, moist and pale. The blood pressure was 80 systolic, 0 diastolic. The pupils were pin point in size and did not react to light. The chest showed dullness and rales in both bases. The heart sounds were distant and weak. A friction rub was heard over the apex, and in the pulmonic area only during expiration. The pulse was weak and irregular, the rate being 120 a minute. The apical impulse was 1 cm outside the left nipple in the fifth interspace. The abdomen was distended and tympanitic. There was slight generalized tenderness without spasm. Peristalsis was normal. The tendon reflexes were markedly reduced or absent.

Examination of the blood showed a white-cell count of 13,400, with 85 per cent neutrophils. The urine was normal. A blood Hinton test was negative. An electrocardiogram showed normal rhythm, with a rate of 120, a PR interval of 0.14 second, upright QRS₁, split QRS₂, slightly depressed ST₁, inverted T₁ and upright T₂.

The patient went steadily downhill. He vomited dark-brown guaiac-positive material. The blood pressure became unobtainable, and the heart sounds were fainter. Peristaltic sounds, which had been present two hours earlier, disappeared. He expired nine hours after admission.

DIFFERENTIAL DIAGNOSIS

DR REED HARWOOD We learn from the record of the first admission the following fairly certain facts: the patient had hypertrophy of the left ventricle, sclerosis of the coronary arteries, with angina pectoris, and probably an old inferior myocardial infarction, as suggested by the electrocardiogram. The cause of the pain that brought him to the hospital is not clear to me, and I gather from the fact that he was allowed to go home in two days that it was decided that he had nothing serious the matter with him. And as happens in so many cases in the practice of medicine, the patient recovered without the luxury of a diagnosis.

Is there anything further stated about the second electrocardiogram?

DR BENJAMIN CASTLEMAN It is a cardiette, and only two leads are reported. Apparently they ran out of paper.

DR HARWOOD That is too bad because I should like to know more about the T waves—particularly those in Lead 4—and to compare them with the previous tracing.

I should also like to know how much guaiac-positive material this patient vomited.

DR CASTLEMAN It says, "He vomited or retched some dark-brown guaiac-positive material." Nothing further is said about it.

DR HARWOOD We have to deal here with the causes of severe, subxiphoid pain, shock and a rapid downhill course in a patient who has been known to have coronary heart disease. Obviously the first cause we think of is acute myocardial infarction. It is not particularly unusual to have upper abdominal pain, instead of the typical substernal pain, as a manifestation of myocardial infarction. There are several aspects of the story that make me wonder if this is the correct diagnosis. In the first place, perspiring for a period of twelve hours before the onset of pain is unusual and makes me think that something else had happened before the painful catastrophe occurred. Secondly, there was no radiation of pain to the arms. Since this patient had had pain in his arms with his attacks of angina, I should have expected a similar pain with myocardial infarction. A friction rub is an ordinary occurrence in myocardial infarction on the second or third day, but the appearance of a friction rub within eighteen hours of the onset of illness is also unusual. The electrocardiogram is not helpful in this case because it is incomplete. It may have been taken too early to record changes that would have been seen at a later date.

There is another possibility that occurs to me. He may have had a myocardial infarction a week or two previous to the onset of the pain. We should have to postulate that this was a silent infarction and that there was some unusual complication that produced death. I am thinking of a rupture of the chordae tendineae or rupture of the ventricle with cardiac tamponade. Under these circumstances I should have expected that the electrocardiogram would have shown more definite changes. Pulmonary embolism is a possibility, but we have no evidence for this, and I do not believe that it is particularly likely.

A dissecting aneurysm with cardiac tamponade is also a possibility. This case reminds me somewhat of that of a patient who was presented here a few weeks ago and who for a week before death had intermittent attacks of rather dull pain low in the neck and just below the xiphoid. With each attack of pain he had profuse perspiration. About three hours before death he developed evidence of occlusion at the bifurcation of the aorta. He died suddenly of cardiac tamponade. In the present case, there is no evidence to substantiate the diagnosis of dissecting aneurysm. There was no evidence of occluded peripheral arteries, and shock, which is usually absent in aneurysm, was present. Death occurred in a matter of hours, rather than in a matter of minutes, the latter being characteristic of cardiac tamponade.

The question to be considered is whether this patient had suffered an abdominal catastrophe to

entistry. It is misleading, however, to imply that the crisis in turning out doctors and dentists is any greater than that in turning out refrigerators — or that it has any more profound or direct effect on the health of the people as a whole

PENICILLIN IN FRIEDLÄNDER-BACILLUS INFECTIONS

A PAPER recently published records a case of *Klebsiella pneumoniae* bacteremia successfully treated by penicillin.¹ This report and even its rather positive title, would be of only minor interest if the case had been presented with the caution, the humility and the reservations that most experienced observers express in reporting a single and inconclusive case. Instead, the authors adopt a rather provocative tone — one of challenge to the wisdom and authority of the combined experience of some of the leading clinical investigators of this country and of Great Britain. They make no attempt to analyze the course and therapy of their case to determine the place that penicillin or other therapeutic measures may have had in the recovery of their patient. They do, however, take great pains to emphasize, "The penicillin was administered in direct contradiction to all published formulae regarding the susceptibility of this organism."

It certainly was not the intention of any workers to be dogmatic or final when they classified various diseases or bacteria according to their susceptibility to penicillin, even the wide variations of different strains of the same organism are well known to such writers. Regarding infections caused by gram-negative bacilli, it is now well known that the Ducrey bacillus is relatively susceptible and clinical reports of favorable effects in the therapy of chancroid have already appeared.²⁻⁵ An occasional strain of the influenza bacillus has also proved slightly sensitive.⁶ Possibly other organisms or isolated strains may also prove to be susceptible. A careful reading of the case report under discussion, however, gives one no reason to believe that the Friedländer bacillus in that case was necessarily susceptible, nor is there any indication that the penicillin was responsible for recovery.

The patient apparently had a posterior pharyngeal abscess and some evidence of increased intracranial pressure, which, in view of the bacteremia, was interpreted as probably due to cavernous sinus phlebitis. There was profuse drainage of purulent exudate from the abscess, either spontaneous or as a result of passing a nasal tube. This drainage in itself might have been enough to account for the recovery, since the prognosis in Friedländer-bacillus bacteremias is most favorable when there is a single accessible focus of infection that can be drained. Thus, there were recoveries in 4 such cases reported from one clinic without the use of specific drugs.⁷ In the present case, however, 5 gm of sodium sulfadiazine was given intravenously soon after admission. Although it is not stated specifically whether sulfadiazine therapy was continued during the penicillin administration, it is not unlikely that more of the sulfonamide was given, and recoveries in severe cases of Friedländer-bacillus infections, including some with bacteremia, treated with sulfonamides alone have been reported.⁸

Although it may be possible that penicillin played some part in the recovery of the patient reported, particularly if there was a mixed infection in which only the Friedländer bacillus was recognized, this can by no means be considered as proved from the data presented. On the basis of this report it would be most hazardous to consider treating a bacteremic case of Friedländer-bacillus infection with penicillin alone. Since penicillin, fortunately, is relatively innocuous even when given in enormous doses, no objection to its use can be offered on that ground. There is the danger, however, of neglecting other more promising and better proved measures, such as the use of sulfadiazine and, particularly, the evacuation of accessible purulent foci, in other words, these procedures, rather than "the contradiction of all published formulae," should be stressed. Although the authors may have gained the distinction of presenting "the first record of a case of *Klebsiella pneumoniae* treated with penicillin," many other cases have undoubtedly been treated by workers who have interpreted their experiences somewhat more cautiously.

It is possible that streptomycin may prove to be effective against Friedländer-bacillus infections,

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FUTURE MEDICAL AND DENTAL EDUCATION

AN AUGUST 21 release by the War Manpower Commission concerns the recruitment of future medical and dental students among the veterans now being discharged from the armed services, it begins with the premise that the Nation is "facing a serious shortage of doctors and dentists in the post-war period." Our editorial eye blinked a little when confronted with this statement, for we had somehow begun to believe that with doctors, as with automobiles, the most serious lack of modern times is here and now—nothing like the numerical shortage of 1945 should recur until another war again calls us forth to battle.

The postwar period, whatever its deficiencies may be, must offer an improvement in the current supply of civilian medical and dental personnel. Both the Army and the Navy have now in their employ a much larger number of physicians and dentists than their peacetime responsibilities, including the best possible care of veterans, should call for. There will inevitably be a return to civilian life of a large number of doctors, along with other personnel. The medical-school facilities of the Nation have been producing graduates at full capacity and at top speed since September, 1941. Although the release states that some medical schools will not fill any substantial part of their first-year classes this fall, such a predicament has not arisen in this region. It must also be remembered that whatever is done to influence the supply of medical schools with students during the current year will not be effective and useful until some time after 1950. An attempt might therefore be made to formulate some clear idea concerning the needs of 1950.

When one contemplates the decades to come, with their new and ever newer remedies, machines and concepts to be applied to less prevalent diseases and, alas, to never changing human nature, one pauses as before an awesome precipice. Where shall we land if we allow ourselves to think only in terms of numbers? Our primary goal for 1950 should be not more doctors but better doctors. It is proper to have quotas for this and that and to take any measures to meet them in wartime, but wartime psychology need not project itself into the future—indeed, it is a little alarming to think of a war manpower commission that seriously concerns itself with what we all hope will be a peacetime economy. Over a long period of years the demand for medical education has been such that standards could be constantly raised. There is no reason to believe that this will not continue. A year of adjustment in which all schools will not be overflowing may occur, but this cannot be anything more than temporary and corresponds to the inevitable change-over that must be undergone by industry.

It is a good thing for the returning veterans to be aware of every opportunity that may be theirs, and they should have good advice, especially those who are contemplating the study of medicine or

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but thus far no reports concerning its clinical use are available

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THE REHABILITATION OF PATIENTS TOTALLY PARALYZED BELOW THE WAIST* WITH SPECIAL REFERENCE TO MAKING THEM AMBULATORY AND CAPABLE OF EARNING THEIR LIVING*

I. Anterior Rhizotomy for Spastic Paraplegia

DONALD MUNRO, M D †

BOSTON

If he has been properly treated, every patient with a spinal-cord or cauda equina injury who is intelligent and co-operative and has the use of the shoulder, arm and hand muscles can be made ambulatory, can have such control of the bladder and bowels as to sleep through the night without either getting up or wetting himself, can carry out ordinary activities throughout the day without soiling himself with feces or having to evacuate his bladder oftener than once every three hours, can lead a normal social life, and within the limits of his intellectual capacity, can earn a satisfactory living. Such patients can start walking without unhealed pressure sores and bedsores and, except for a small group, without the need for an inlying catheter or any substitute therefor. They have to use crutches and to wear, when ambulatory, caliper walking splints, which, however, permit them to stand or sit. These are the only restrictions to their living the same social life and having the same earning capacity that they had before becoming paralyzed.

This paper is the first of a series that describes certain therapeutic procedures that have made the attainment of these end results possible. Although my experience has been largely limited to civilian casualties of this type, there is no reason why the lessons learned there should not be applied to the war casualties of the same class.

The material analyzed in the various papers has been taken from a series of 243 patients suffering from various types of cord disease (Table 1). Most of them had had an injury to the cord or cauda equina. One hundred and thirty-five patients with cervical-cord injury are not included in this table because only 2 patients with transection lived long

enough to permit adequate study. Although the most frequent symptom in the classified patients was total voluntary paralysis below the waist and the rarest one uncomplicated bladder dysfunction, the majority of patients had a combination of

TABLE 1 Classification of 98 Cases of Cord Disease

CLASSIFICATION	LOCALIZATION			ALL CASES
	DORSO-LUMBAR	SACRAL	CAUDA EQUINAL	
Permanent functional loss				
Total voluntary paralysis	51	4	4	59
Partial voluntary paralysis	4	6	7	17
Bladder dysfunction	0	1	2	3
Disabling pain	0	0	6	6
Transitory symptoms	7	0	6	13
Pathology				
Injury	57	11	25	93
Epidural spinal abscess	3	0	0	3
Intraspinal tumor	2	0	0	2
Totals	62	11	25	98

conditions. These patients are classified as they are in Table 1 because motor paralysis, total or partial, was the outstanding symptom in one group, just as bladder dysfunction and pain were the outstanding symptoms in the other groups.

The 59 cases chosen for analysis from this series were picked according to the following criteria. The patient must have lived for at least ninety days after the onset of the disease or the sustaining of the accident. He must have been rendered incapable of doing gainful labor, or its equivalent in the case of a housewife or child, by the injury or disease. Lastly, the lesion must have been at or below the second thoracic segment of the spinal cord.

Total useful voluntary motor and sensory paralysis starting at some point below the waist may be caused by a complete anatomic transection of the thoracolumbar cord below the second thoracic segment, by a partial anatomic transection of the thoracolumbar cord, which is nevertheless functionally so complete as to deprive the patient of

*From the Department of Neurosurgery, Boston City Hospital. Presented in part before a meeting of the Department of Veterans' Affairs at Toronto, Canada, January 18 and 19, 1945.

†Assistant professor of neurosurgery, Harvard Medical School, associate professor of neurosurgery, Boston University School of Medicine, chief Department of Neurosurgery, Boston City Hospital.

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DEATHS

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September 15 He was in his fifty-ninth year
Dr Buck received his degree from Bowdoin Medical School,
in 1914
His widow survives

DAVISON — Arthur H Davison, M D, of Milton, died
September 26 He was in his seventy-second year
Dr Davison received his degree from Harvard Medical
School in 1902 He was medical director of the Boston Mutual
Life Insurance Company and a former member of the Milton
Hospital staff
His widow, a daughter and a son survive

LIBBY — J Herbert Libby, M D, of East Weymouth,
died September 25 He was in his seventy-ninth year
Dr Libby received his degree from Harvard Medical
School in 1892 He retired in 1942 He was a fellow of the
American Medical Association

MISCELLANY

MAJOR HALSTED AWARDED LEGION OF MERIT

Major James A Halsted, M C, A U S, on leave of absence
as a member of the Medical Staff of the Massachusetts
General Hospital, was recently awarded the Legion of Merit
"for exceptionally meritorious conduct" The citation reads
in part

Major Halsted, by his continuous study of the problem
of gastrointestinal disorders in combat soldiers, evolved
new methods of treatment which decreased the average
hospitalization time from twenty-five days to six, and
enabled the medical corps to return 80 per cent of such
cases to full combat duty, whereas formerly only 40 per
cent could be returned

(Notices on page xvii)

and flexors of the opposite thigh. I have never seen an extension of the opposite thigh as a continuation of the original flexion response in the stimulated leg. The flexor and adductor muscles in both legs are hypertonic, and the usual flexor tendon reflexes, such as those of the hamstrings, are extremely active. The extensor tendon reflexes, such as the knee and ankle jerks, are hyperactive unless the muscle is stretched so tightly as to interfere mechanically with its contraction. The extensor

pressure points and splinting has to be abandoned. Thus, unless it can be corrected the paraplegia in flexion of itself prevents ambulation.

In addition, and more importantly, the contraction of the abdominal muscles, which occurs as part of the mass reflex (except as noted above), stimulates the urinary bladder and causes it to expel its contents irrespective of amount. If an indwelling catheter is in place, and whether or not tidal drainage is in use, the urine leaves the bladder around the catheter as well as through it because of the suddenness, rapidity and force of the detrusor contraction. These patients cannot be kept dry by any method and cannot be trained to control their urinary outflow so long as the mass reflex remains active. They develop pressure sores and bedsores and are constantly wet and soiled. Social life is impossible and they are soon moved out of their homes and relegated to a nursing home or public institution, where they remain until they die, usually of some intercurrent infection. Long before that happens, however, their morale has vanished and death comes as a relief.

If the mass reflex and its effects can be counteracted, splints can be applied that will permit such a patient to be ambulatory. The bladder and bowels can also be brought sufficiently under control so that the patient can be trained to go through the night without getting wet and without waking, and through the day without getting soiled and without having to empty his bladder oftener than once every three hours. This permits him to be not only ambulatory but self-supporting as well. Because I believe that the logical point of any attack designed to eliminate this abnormal reflex response is on the motor side of the reflex arc, an operation has been developed that not only changes this hypertonic spastic paraplegia to one of a flaccid type but also prevents the spreading to the abdominal muscles of any reflex motor activity in the extremities, and thus allows for control of the bladder. This is accomplished by the intraspinal division of the proper anterior spinal roots. This is preferred to division of the posterior roots because it attacks the problem, especially that of the bladder, more directly. All anterior roots are cut bilaterally from the tenth or eleventh thoracic segment through the first sacral segment. If the rhizotomy is complete, the lower abdominal and psoas muscles, the lower part of the erector spinae group and all the muscles of the lower legs become flaccid, and flexion and adduction contractures straighten out (Figs 2 and 3). Any local tendon shortening that remains can be cared for by manipulation or a tenotomy. By the use of appropriate splints the legs can then be stabilized and hence made capable of bearing weight. With the help of crutches such patients can learn to walk and to be normally active within the limits imposed by the splints. Because the

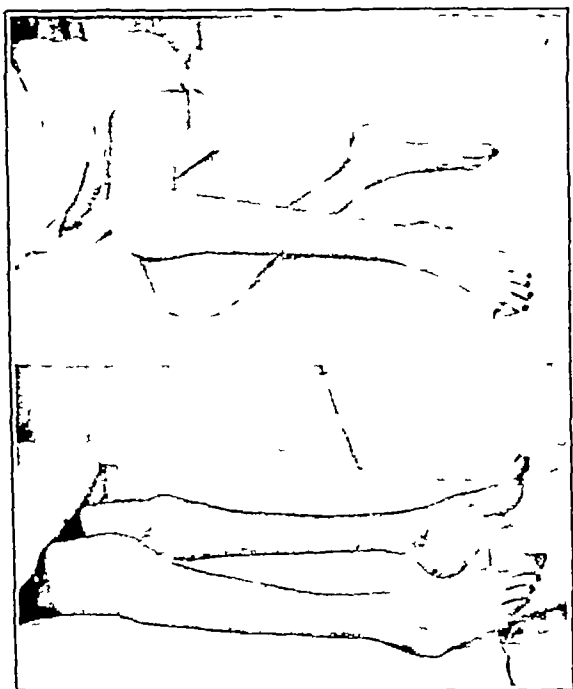


FIGURE 2

This was a patient, aged fifteen, who had a transverse myelitis and an anatomic transection at the level of the fifth and sixth dorsal segments, caused by an epidural spinal abscess. The photographs show the mass reflex previous to dorsolumbar anterior rhizotomy and its disappearance after operation.

group of muscles themselves are not usually otherwise hypertonic. I have seen no such case with an extensor thrust.² Long-standing cases show extreme flexor and adductor contractures and may, unless protection is provided, develop pressure sores on the medial aspects of the knees, over the patellas and on the chest wall from constant contact between the knees themselves and between the patellas and the chest wall. Massage and manipulation and especially forcible extension and abduction of the legs lead to nothing but further increased flexion and adduction and greater contractive effort on the part of these muscles. Splinting designed to maintain the legs or feet in extension or in a position of use acts in the same way that manipulation does. If it is effective, sores develop at all

all useful motor or sensory control of the bladder and rectum and all or part of the muscles of the lower abdomen, low back and legs—functional transection, by destruction of the sacral cord and adjoining cauda equina, or by destruction or compression of the cauda equina alone. This paper concerns itself only with the first group (complete anatomic transection below the second thoracic segment), and discusses a method by which the spastic paraplegia that is associated with this lesion and that cannot be splinted can be altered to a flaccid paraplegia that can be

ANATOMIC TRANSECTION OF THE CORD BETWEEN THE SECOND THORACIC AND FIRST SACRAL SEGMENTS

Patients whose cords have been completely and anatomically transected between the second thoracic and the first sacral segment develop a so-called "mass reflex" or "maximal flexor response to a minimal sensory stimulus" below the level of cord injury as soon as they have recovered from the effects of spinal shock, provided that their nourishment is kept up and that no genitourinary-tract or other major infection or toxic state is present. The classic so-called "paraplegia in flexion" is present (Fig 1) (There were 19 such patients in this group of 59). There is a complete absence of all voluntary motion, a total loss of all sensory appreciation and a reversion of the bladder and rectum to a pure reflex mechanism. When the mass reflex is fully developed, the patients are so deformed that they cannot sit up in a wheel chair, much less stand erect. Under the usual methods of treatment, the bladder discharges at the slightest stimulus—such, for example, as a cold draft or a jarring of the bed,—the bowels empty at unpredictable intervals, and the patient is constantly wet or soiled, requires an inordinate amount of nursing and develops intractable pressure sores and bedsores in spite of all care. He not only cannot support himself but is a constant and severe financial drain on his friends and relatives. Such patients are social pariahs in their own sight and in that of everyone associated with them.

Despite this usual sequence of events, such transection of the thoracolumbar cord need not necessarily condemn the patient to a bedridden, filthy life. The physician and his patient should clearly appreciate that even with this severe anatomic lesion, ambulation and normal social activity can and will be the ultimate result, provided that they both have the necessary patience and give the endless attention to the details of the preliminary treatment that is so essential while the patient is necessarily bedridden and that make equally important definitive procedures possible later. This subject has been discussed elsewhere¹ and need not be dealt with again here. Suffice it to say that,

by the time the patient's bone injury has healed sufficiently to permit him to stand upright without danger of collapse of the spinal column, he should have developed a reflex bladder without evidence of genitourinary-tract infection or stone



FIGURE 1

This patient, aged seventeen years, had an anatomic transection at the level of the fourth and fifth thoracic segments caused by concussion of the cord from a bullet wound of the body of the fourth thoracic vertebra. An active mass reflex, with adductor flexor contractions and deformity was present, and his condition before a dorsolumbar anterior rhizotomy is illustrated.

formation, his bedsores, if he has had any, should be healing and his pressure sores stationary, the serum protein should be normal, the state of nutrition satisfactory, the temperature and pulse normal, and the strength of the arms and shoulders developed well beyond the pre-injury level.

An active mass reflex in its classic manifestation takes the form of a dorsiflexion of the great toe, a flexion of the ankle and knee, an adduction and flexion of the hip (Fig 2) and, unless the peripheral nerves that supply them have been destroyed, contraction of the lower abdominal and spinal muscles, possibly with a spread to the adductor

two potent sources of sepsis and death. The relation of the first lumbar root to the last dentate ligament proved to be the key to the accurate identification of the roots to be sectioned, and the solution of the problems that arose out of hitherto uncontrollable infections was reached in the course of the next seven years. In the four years since 1940 sepsis of the genitourinary tract has to all intents and purposes ceased to exist in patients with spinal-cord injuries in my clinic.³⁻⁵ It should be emphasized that in 102 patients who needed and were treated by tidal drainage, only 2 left the hospital with demonstrable evidence, including urine culture, of genitourinary-tract infection, whereas of 37 patients who needed tidal drainage but did not get it, 11 were discharged with obvious genitourinary-tract infection. Of course, tidal drainage cannot be used under combat conditions or ordinarily while the patient is being transported by air or overseas. It should be provided, however, just as soon as the wounded man has reached the hospital where definitive treatment is to be given.

The only complication that has arisen in this field is the rare formation of bladder calculi. In the past year this also appears to have been eliminated by the use of Solutions M or G as irrigating fluids.⁶

During this same period pressure sores and bedsores and the infection caused by them have also been virtually eliminated in this general group of patients.^{1, 7} The incidence of bedsores developing during hospitalization dropped from 16 in 146 patients from 1930 to 1940 to 7 in 87 from 1940 to 1945. During the same periods, whereas 5 per cent of the former group were discharged with their bedsores unhealed, only 1 per cent of the latter left with the same condition. Patients admitted with bedsores already present during these two periods each made up 7 per cent of their respective groups. With these sources of trouble cared for, it was possible to resume investigation into the effects of an anterior dorsolumbar rhizotomy with a more satisfactory technic. A description of the operation as it is now performed follows.

DORSOLUMBAR ANTERIOR RHIZOTOMY

In dorsolumbar anterior rhizotomy, the spinous process of the twelfth thoracic vertebra is identified. A bilateral laminectomy of the eleventh and twelfth thoracic vertebra is done. The dura is opened enough to see whether the conus and the start of the cauda have been exposed. If the exposure is too high, the next lowest laminae, which should be those of the first lumbar vertebra, are removed. If it is just right or too low, the laminae of the tenth thoracic vertebra, the next highest pair, are removed. After hemostasis the dura is opened for the full length of the wound. The arachnoid is then opened, and the subarachnoid space is emptied. The operator must be sure that the lumbar and sacral cord,

the conus and the upper end of the cauda are exposed. The arachnoid is torn into laterally to expose the last dentate ligament (fig 4) on one side. If it is absent on one side it is looked for on the other. The intraspinal nerve (combined posterior and anterior roots) that encloses it (the ligament) and leaves by the dural opening next below is picked up and marked with a silver clip close to its point of exit through the dura. This is the first lumbar root. Then the next highest lateral projection of the dentate ligament is isolated. A silk stitch is

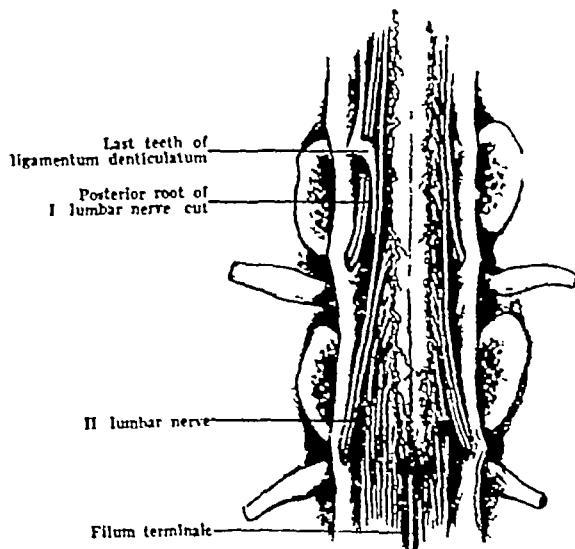


FIGURE 4

The relation of the last dentate ligament to the first lumbar roots (reprinted from Frazier and Allen¹⁰ by permission of the publisher)

put through each of these projections, and they are cut free from their dural attachments. These stitches are used as handles to rotate the cord so that the full length of the dentate ligament and the line of separation between the exit of the posterior and anterior roots from the cord can be seen.

The anterior component of the first lumbar root (identified above) is picked up, a silver clip is put on it about midway between the point where the individual filaments unite to form a single strand and its point of exit through the dura, and the root is cut lateral to the clip. The medial portion of the cut root is pulled laterally, this part can be identified by the clip on it. The traction delimits the upper fibers of origin of the next lower and the lower fibers of origin of the next higher anterior root. By following these laterally the trunks of the anterior roots of the twelfth thoracic and the second lumbar nerves can be identified and cut. By repeating this traction with each succeeding root all the other anterior roots can be identified and cut one by one. A return to the first lumbar root, which still has a clip on it, will serve for re-orientation should this be necessary. If the point

bladder no longer empties except when it reaches its critical amount of filling or when it is deliberately stimulated, the patients also remain dry after they have learned how to urinate by the clock. For the same reason it is possible to train them so that their bowels empty themselves at the same hour once a day or once every two days. Soiling at unexpected times, with its attendant discomfort and embarrassment, is thus done away with.

This operation was first attempted in 1933 and again in 1934. Both patients had active mass re-

and rectum under sufficient control so that he could go out. Because both patients still got wet without tidal drainage, they had to use it constantly. One progressed satisfactorily at home with this limited life until his physician decided to discard the tidal drainage. He thereupon died from sepsis of the genitourinary tract. The other patient never left the hospital and also died of sepsis, which originated in a bed sore over one trochanter and led to osteomyelitis of the femur and ilium. Although the operation was far from successful, it

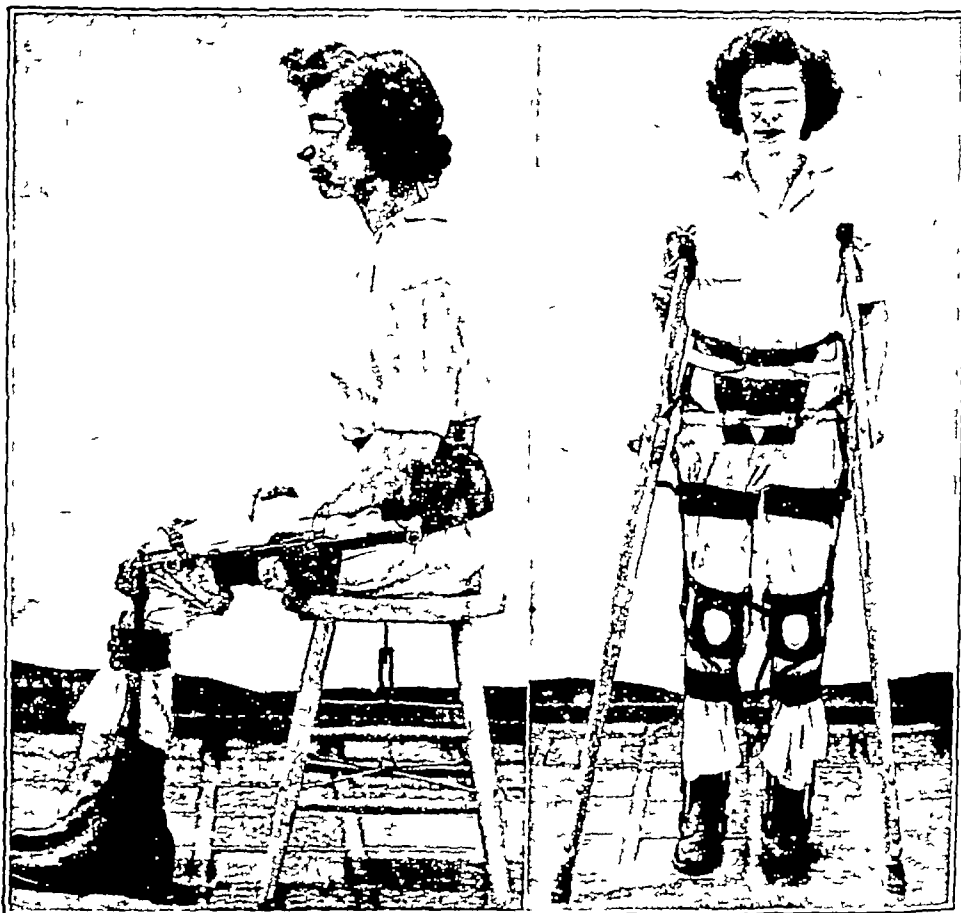


FIGURE 3

This is the same patient shown in Figure 2. She is fully active in splints and with the aid of crutches, and has complete control of the bladder and bowel.

flexes and crippling adduction-flexion deformities and had been bedridden for two and a half years. Identification of the roots to be cut was attempted by counting upward from what was thought to be the fifth sacral root. This method was recognized as necessarily inaccurate—an impression that has since been verified. As a result, the relief obtained in both these cases was only partial. With the aid of tenotomies it was enough, however, to correct the flexion and adduction deformities. Both patients could be mobilized in wheel chairs, and one went home. Neither, however, could bring his bladder

was apparent from these cases that it was worth perfecting and probably could do what was expected of it.

For this operation to be most effective a more exact method of identifying the roots was obviously necessary. It was also apparent that in addition the problems of genitourinary-tract infection and the prevention of bedsores had to be met and solved. It would be of little use to put a patient into such shape that he could become ambulatory with the aid of splints if the attainment of this end was to be denied him because of lack of control over these

This subject will be discussed in more detail in a later paper. Because one of the prime purposes of performing an anterior rhizotomy is to enable the patient to regain control of the bladder, and since the difference between Head's conclusions and my observations relative to this phase of the mass reflex is one of explanation rather than one of fact, this is of less practical importance in relation to doing this operation than it appears to be.

It cannot be emphasized too strongly that the fundamental requirements prior to rhizotomy are a complete absence of voluntary motor power, a complete loss of all forms of sensory perception, a predominantly flexor or flexor-adductor contraction in the abdominal muscles and in each leg in response to a noxious stimulus applied to the sole of either foot, and the emptying of the bladder as an accompaniment of the majority of such phenomena or in response to other less noxious and more varied stimuli. On the other hand, this should not be taken to mean that the demonstration of such phenomena *necessitates* a rhizotomy to relieve the patient of his distressing or disabling symptoms. I have relieved 1 patient (not included as one of the group with an anatomic transection) with all the motor and bladder characteristics of the mass reflex by decompressing the middle thoracic cord and relieving it of the pressure exerted on it by an extradural malignant tumor. Although neither voluntary motion nor sensation returned postoperatively, so far as any observation short of post-mortem examination went the cord appeared to be entirely normal. Instead of the spastic paraplegia and mass reflex that was actually present and presumably indicated an anatomic transection, the patient should have had the flaccid paraplegia of a physiologic transection before as well as after the operation.

A shrunken or hypertrophied bladder, such as is associated with prolonged suprapubic or urethral catheter drainage, may give every appearance of being a mass-reflex bladder, when in fact it is not. If the patient happens to have a total sensory and voluntary motor paralysis as well, the symptoms may be interpreted as representing a partial mass reflex. A rhizotomy under such circumstances is entirely unnecessary, and even if performed will not replace the essential stretching and retraining of the bladder that alone will effect a correction of the urinary symptoms.

The mass reflex may come on slowly and build itself up over a period of weeks. In a patient whose upper thoracic transverse myelitis and anatomic transection were caused by an epidural spinal abscess, the classic mass-reflex response did not appear until three months after the abscess had been drained and the wound had healed except for epithelialization. Clinically, the patient had presented no evidence of toxic absorption for a long time previous to this. Only one leg, however, showed

the mass-reflex response at that time. Two weeks later the other leg developed mass-reflex responses, and it was not until one month later that the bladder first began to overflow in connection with these involuntary movements (Fig 5). Following rhizot-



FIGURE 5

This patient, aged thirty-six years, had a transverse myelitis and anatomic transection at the level of the eighth to tenth thoracic segments caused by an epidural spinal abscess, which was drained on July 31, 1944. A flexor response developed in the left leg on October 31, and in both legs on November 14. The bladder component of the mass reflex was added to this on December 17. A dorsolumbar anterior rhizotomy was done on December 20. The three photographs show, respectively, the unilateral flexor response, the bilateral flexor response and the condition after operation.

omy the spastic paraplegia became flaccid, and sufficient control was promptly established over the bladder so that it emptied only in response to a given constant amount of fill and stretch or to

of exit of any root is in question, the posterior portion of the first lumbar root, which has a clip on it next to the dura, serves as a reliable starting point for identification. All anterior roots from the eleventh thoracic through the first sacral should be cut and if possible that of the tenth thoracic also, but never under any circumstances should the roots below the first sacral be divided. All the blood vessels that can be spared should be saved. If a vessel cannot be spared it should be closed with the Bovie cutting current, no attention being paid to the resulting muscular contractions. Two blunt hooks should be available to handle the uncut nerves.

After sectioning of the desired anterior roots, all the medial portions should be pulled laterally and laid out in order and in such a way that they can be inspected from their points of origin on the cord to their points of section. The operator must make sure that no roots have been missed. The latter is easy to do, but this method of inspection makes it at once evident if a root has not been cut that should have been. I have never had to cut any posterior roots, but see no reason why this cannot be done if it is absolutely necessary. Anterior roots can be differentiated from posterior roots by squeezing them gently and noting the resultant motor activity.

After all the proper anterior roots have been cut on one side, the process as outlined above should be repeated on the other side. The operator should *not*, however, take off the silver clips or take out the dentate ligament stitches on the first side until the second is finished. They may be needed to identify roots on the second side that cannot be otherwise placed, or to rotate the cord. After the operator has satisfied himself that all the proper roots have been cut that should be, then, and only then should the clips be removed and the silk stitches pulled out. The dura should be closed tightly and the wound closed in layers without drainage.

If the patient is so deformed that the legs cannot be straightened, the laminectomy should be done in the lumbar-puncture position. If this position is used, pads must be placed under the patient's flank to make the spine level. If this is not done it may be impossible to identify the structures sufficiently accurately even to expose the laminae.

I prefer intravenous Pentothal Sodium on an avertin base as an anesthetic. Blood should be available for transfusion during operation, — since many of these patients do not stand a long operation well. The operator should not hesitate to include part of any old laminectomy scar in the new incision, but should first identify the structures in the unoperated part of the field. When previous laminectomies have been done, it is worth while to take particular pains to identify the spinous process of the twelfth thoracic vertebra before starting to operate. Errors either way in locating the center point of the incision will prolong the operation and result

in unnecessary removal of a large amount of bone. After operation these patients redevelop an atonic bladder for a variable length of time. This should be cared for at once to avoid damage to the bladder wall by overdistention.

A flaccid paralysis of the legs, low back and low abdomen should be demonstrable at once after operation. It should be permanent. If spasticity redevelops, too few roots have been cut.

Operators inexperienced in neurosurgical technique should not attempt this procedure without considerable preliminary training.

DISCUSSION

Because this operation is a permanently destructive one, the indications for performing it should never be considered lightly. For the present, at least, it should be strictly limited to those patients whose cord is anatomically transected and in whom all neural connections between the cut surfaces of the cord have been destroyed. This condition may not be easy to recognize by any means short of postmortem examination. Among other things the presence of deforming flexor and adductor spastic contractures, with the resultant impossibility of applying splints that permit weight-bearing, is not by any means conclusive evidence that such an injury exists, and does not of itself warrant a root section in the absence of more certain and fundamental evidence that the cord has actually been transected.

Among others, Head² has pointed out that in a true mass reflex the positive motor activity is restricted to the flexor muscles. It makes its earliest appearance as a dorsiflexion of the great toe (Babinski reflex) or as a contraction of the hamstrings, spreading later to include the other flexor muscles of the leg, the muscles of the anterior abdominal wall and occasionally the flexors of the other leg. (My experience indicates that the psoas and iliacus muscles should be added to this group.) Head holds that this is not a part of the normal postural reflexes but belongs to the ancient nociceptive mechanism, and further contends that reflex extension is evidence of incomplete transection. My experience with 51 patients with dorsolumbar cord injuries, all of whom had total voluntary motor paralysis below the level of injury, 37 of whom lived long enough to warrant attaching any significance to observations made on them and 19 of whom had a mass reflex as described above in agreement in so far as the motor paralysis, the elicitation of the reflex and the spread of the motor response to noxious stimuli applied below the injured segment go. I have been unable to verify Head's conclusion relative to the facilitating of bladder emptying, however, in these and some 177 other patients with injuries to the cord and cauda equina of all degrees of severity and at all levels from the fourth cervical segment downward.

sufficient roots were cut. In all the patients the pre-operative deforming flexion-adduction spastic paraplegia has been changed to a nondeforming flaccid paraplegia. The irregular bladder emptying that kept the patient constantly wet, proved a difficult and often impossible nursing problem, led the patient to seclude himself and prevented him from carrying out any social activity, ambulation or self-support, it has been so altered that twenty-four-hour control without the use of either a urethral catheter or suprapubic drainage has been or is about to be attained in all but the first two patients. Bedsores have been healed and pressure sores have been either healed or arrested before operation in every case. No bedsores or pressure sores have developed after operation, and no complications traceable to the operative procedure have developed. Two patients have learned so to control their bowels that defecation occurs only once a day at a predetermined hour. Three others are well on the way toward attaining this end. The remainder have not done so either because—as in 4 cases—insufficient time has elapsed or because—as in 1 case—the patient did not have sufficient mental equipment to learn to do so. All but the first two either can be or have been equipped with caliper splints preparatory to ambulation and are either walking or learning to do so. The indications for the operation given above were strictly adhered to. All but one patient had an exploratory or therapeutic laminectomy over the site of the cord injury preliminary to the rhizotomy.

There were 2 other patients with anatomic cord transections and spastic paraplegia that were not considered suitable for rhizotomy. In one case the spinal nerves that innervated the abdominal muscles had been destroyed bilaterally as part of the injury that transected the cord. Because of this deficit this patient has been able to establish a workable although incomplete bladder control. After eight years of genitourinary-tract infection and resultant inhibition of the mass reflex, proper and persistent training has finally made splinting and ambulation also possible, despite the presence of a demonstrable but not particularly active characteristic mass reflex. Constant intelligent care has also prevented the development of deformities and pressure sores. Control of the bowels is maintained with the help of enemas. Under the circumstances, rhizotomy could add little or nothing to this patient's mobility and was considered inadvisable. The other patient presented all the indications for rhizotomy, but because she was a moron and incapable of such co-operation as would

have been necessary to teach her to control her bladder and learn to walk, her family was advised not to have a rhizotomy performed.

A third patient who had a transected cord but did not have a rhizotomy was able to lead a wheelchair life in spite of a spastic paraplegia and moderate but not disabling flexion-adduction deformities of the legs. Bladder control was absent. The mass reflex was characteristic and active, and rhizotomy was advised, but the patient refused it. Another similar patient preferred life in a public institution to rhizotomy and also refused operation.

Five early cases were not operated on because of inability to control sepsis and hypoproteinemia before they died.

SUMMARY

Bilateral intraspinal division of the anterior roots of the eleventh thoracic through the first sacral spinal nerves is recommended as a means of changing a spastic to a flaccid paraplegia in patients with an anatomic transection of the spinal cord at any point between the second thoracic and the second-sacral segments preliminary to making the patients ambulant and to providing them with complete twenty-four-hour control of micturition so that they may again become active members of their community and be self-supporting.

The need for establishing certain stringent pre-operative indications is emphasized. These requirements are described, and certain confusing aspects of them are discussed.

The technic of the operation is described.

The application and results of the operation in 10 of 19 patients with spastic paraplegia following anatomic transection of the spinal cord are reported.

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some such purposeful external stimulus as abdominal massage

The absence of an extensor thrust or of a response on the part of the extensor muscles of the legs to a stimulus of the thigh, groins or abdominal wall with primary extension of all joints of the lower extremity, as described by Head² and considered by him to be incompatible with a mass reflex, did *not* mean in this group of 59 patients that a mass reflex would develop later or that there was an anatomic transection of the cord. Nor, in my experience, is an extensor thrust a prerequisite to a diagnosis that predicates neural connections between the parts of the cord that are above and below the damaged area. In 18 totally paralyzed patients who had a physiologic transection, who did *not* have a mass reflex and who survived an injury to the thoracic cord long enough to warrant significant observations, neither of the above phenomena was ever demonstrable. Of 12 of these that have permanent total flaccid paraplegia, 7 are earning their living, 2 are ambulant but not working, and 3 left the hospital to take up wheelchair lives. One of the patients who is working first developed an extensor thrust three and a half years after injury. In the meantime, he had left the hospital and been active with the aid of splints and crutches for eight months. He had been free of bedsores and genitourinary-tract infection and had had twenty-four-hour control of the bladder without a catheter for one year previous to the development of this phenomenon. Its presence now interferes in no way with his activities. Of the remaining 6 patients, 2 are on the ward, 3 died in the hospital, and 1 refused treatment. On the other hand, 2 other patients not included in the above group, — one with a cervical hematomyelia and the other with a midthoracic injury, — both of whom retained partial sensation and voluntary motor power below the level of the cord injury, have had not only a classic extensor thrust² and primary extension of the joints of the extremities, but also uncontrollable and unpredictable flexor and extensor spasms of the muscles of the legs and abdomen. I have been unable to find any previous description of this condition. This is not without its importance, because on superficial examination it could easily be confused with a true mass reflex. Another patient (included among the 10 receiving rhizotomies) who was known to have a complete absence of cord tissue for a distance of 2 cm. in the midthoracic region as the result of a shell wound showed the classic adductor-flexor mass-reflex response, as well as "primary extension of all joints of the lower extremity" on stimulation of the thighs, groins and soles of the feet. He did not, however, have an extensor thrust. All these responses were abolished after anterior rhizotomy. My experience strongly suggests, therefore, that neither the presence nor the absence of reflex activity in the extensor

muscles below the level of the cord injury, even in the presence of total sensory and voluntary motor paralysis, should necessarily be considered an indication of an anatomic cord transection, and hence has no bearing on the problem of whether a given patient needs an anterior rhizotomy.

Perhaps the most important prerequisite to making such a decision, and certainly the most important one in estimating the significance of the neurologic signs that are demonstrable, is the certainty that all infections or conditions that lead to infection or toxicity in the patient are done away with. Indeed, the importance of this cannot be overstressed. Furthermore, this requirement will not necessarily or often be met by anything short of a return to normalcy of certain fundamental needs of the patient's metabolism. First, there must be no evidence of genitourinary-tract infection other than a culturable bacteriuria, and that only when an indwelling catheter is in use. Pyelitis, cystitis or calculi anywhere in the genitourinary tract, as shown by clumped leukocytes, constant albuminuria, concentrated urine or other clinical evidence, may alter the characteristics of the mass reflex to any degree from complete abolition to the most minor changes and do away with the diagnostic significance of whatever neurologic changes are present. The same effect may be produced by the presence of unhealed and, more particularly, advancing bedsores and pressure sores. Spinal shock, anemia, hypoproteinemia, undernourishment, avitaminosis and the like all exert a similar effect. All these must be corrected and the patient maintained at normalcy before a decision can be reached relative to the need for an anterior rhizotomy.

Visualization of the injured area of the cord as a means of determining whether the latter is anatomically transected does not necessarily settle this question. I⁸ have shown that what appeared to be intact areas in the cord exposed at operation proved later at autopsy and by clinical standards to be actually anatomic transections, whereas not a few patients with a quadriplegia that came on practically simultaneously with the accident have later walked out of the hospital and again started earning their living.⁹ My experience leads me to believe, however, that no harm will follow and much good may come from a laminectomy done to relieve a spinal subarachnoid block at the site of injury — particularly if a decompression is provided early. Moreover, I believe that any patient who has both a mass reflex and a spinal subarachnoid block should have the block relieved by a decompressive laminectomy before being subjected to an anterior rhizotomy.

RESULTS

I have performed a bilateral dorsolumbar anterior rhizotomy as described above on 10 patients. One patient was operated on three times before suf-

Groups 1 and 2, nitroglycerin was considerably more effective (Table 1) On the other hand,

TABLE 1 *Comparative Effect of Nitroglycerin and Cobra Venom on the Standardized Tolerance of Patients with Angina Pectoris*

CASE NO	NO MEDICATION	TWO MINUTES AFTER SUBLINGUAL ADMINISTRATION OF NITROGLYCERIN	AFTER THREE OR MORE INJECTIONS OF COBRA VENOM
Group 1			
1	24	36	44
2	35	75	48
3	40	108	42
4	20	44	35
Group 2			
5	20	32	41
6	45	62	51
7	36	44	30
Group 3			
8	4	4	13
9	10	10	20
10	11		20
11	20	20	28
12	40	41	35

in 3 of the 5 patients comprising Group 3 the injection of cobra venom resulted in a significant increase in ability to do work. In 2 of these patients

times daily. The usual amount of exercise under the standardized conditions necessary to induce angina was twenty to twenty-five trips. Following the administration of nitroglycerin the patient was able to do thirty-two trips. Treatment with cobra venom was begun with a single dose of 10 mouse units. The exercise tolerance and the clinical course remained unchanged during the next fourteen days. Thereafter daily injections of 10 mouse units each were given. On the fifth day a marked rise in exercise tolerance occurred, and the patient experienced no pain during her daily routine. After seven injections of cobra venom, daily injections of saline solution were substituted. During the next eleven days there were no attacks in daily life. Because the standardized exercise tolerance seemed to be decreasing, a second course of seven daily injections of cobra venom (10 mouse units) was given. Again improvement was observed, beginning on the fifth day. Six days after discontinuing medication, a decrease in exercise tolerance was observed. By the

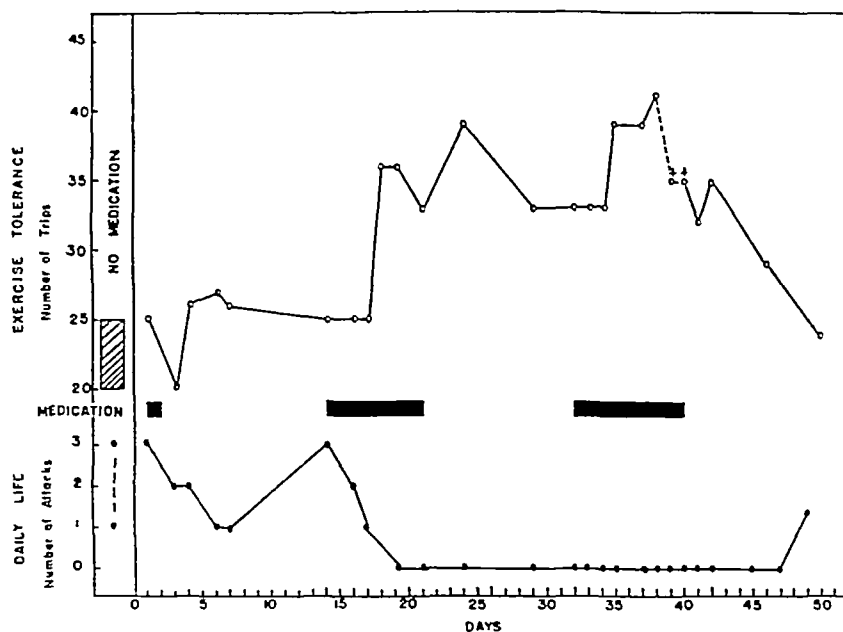


FIGURE 1 *The Effect of Cobra Venom on the Exercise Tolerance and the Number of Attacks of Pain in Daily Life in Case 5*

cobra venom is the only drug out of fifty-seven tested to date that has enabled them to do more work or has resulted in demonstrable clinical improvement. The increase in ability to do work under standardized conditions was paralleled by a decrease in the frequency of attacks in daily life.

The effect of cobra venom is best illustrated by the results in Case 5 (Fig 1). This patient, a 69-year-old widow, had had angina pectoris for seven years and had been observed in the Angina Clinic for five years. Attacks usually occurred one to three

ninth day the exercise tolerance had returned to the control levels and attacks in daily life returned.

Effect on Electrocardiogram after Exercise

Electrocardiographic studies^{12, 13} were carried out in 2 of the 7 patients who benefited by the injection of cobra venom, and the results were compared with those observed following the administration of nitroglycerin. In contrast to the effect of nitroglycerin, cobra venom did not prevent the electrocardiographic changes induced by exercise. Despite the

COBRA VENOM IN THE TREATMENT OF ANGINA PECTORIS*

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BOSTON

THE usefulness of cobra venom for the control of pain was first suggested in 1929 by Monacless¹. In 1936, Bullrich² reported favorable results in the treatment of angina pectoris. Seven patients — 5 with syphilitic aortitis and 2 with coronary arteriosclerosis — received 125 to 50 mouse units§ of cobra venom intravenously, the succeeding doses and frequency of administration varied in each case. The physiologic and pharmacodynamic effects of cobra venom have been investigated by Macht,^{3,4} who demonstrated that its effects were those of a sedative acting on the thalamus. He⁵ reported relief of various types of pain in approximately 70 per cent of 200 patients, including 2 with angina pectoris. The method and duration of administration in these 2 cases were not described. In 1940, Parsonnet and Bernstein⁶ used cobra venom successfully in 5 patients with stenocardia at rest unrelieved by any medication except morphine sulfate. The medication was given intramuscularly in doses of 5 to 10 mouse units daily for three to five days, then 10 units every other day for five or six doses and finally 5 units once or twice weekly. In 3 cases complete disappearance of pain occurred after two, three and five days, respectively. In 4 patients no further attacks at rest were experienced, although 2 of these had pain on exertion, in the remaining case pain returned on two subsequent occasions but was relieved each time by an additional course of treatment.

The literature thus records 14 cases of angina pectoris treated by the injection of cobra venom with uniformly good results. It must be pointed out that all three investigators evaluated the benefits of therapy by the clinical history alone. The clinical evaluation of therapy in angina pectoris is, however, difficult because of the natural variation in the course of the disease and because psychologic factors cannot be adequately controlled. It has been repeatedly demonstrated that when judged by the clinical history, beneficial results can be obtained with the use of placebos as frequently as with other medication,⁷⁻⁹ so that objective studies are necessary. The present study was undertaken as part of an objective evaluation of methods of treatment in this condition, which has up to the present included approximately seventy different therapeutic measures.¹⁰

MATERIAL AND METHODS

Twelve patients — 10 men and 2 women — with angina pectoris of coronary arteriosclerotic origin had been studied for various periods of time — 9 cases for two to seven years and 3 cases for two to four months in a special clinic devoted to angina pectoris. During the period of observation the frequency of the attacks in daily life became well known. The amount of work that could be performed under standardized conditions before pain developed had been determined on many occasions according to the method previously presented.¹¹ The patients' responses to many different methods of therapy were established. Four responded strikingly to many different forms of treatment. Following the sublingual administration of 0.3 mg of nitroglycerin they were able to do 100 per cent more work than was possible without medication, and according to the scheme previously described¹⁰ they were classified as Group 1 patients (marked reactors). Three of the patients responded in a moderate degree to therapy in that they were able to do approximately 50 per cent more work after nitroglycerin, and were termed Group 2 patients (moderate reactors). The remaining 5 patients failed to respond to any of the usual methods of treatment, including nitroglycerin, and were termed Group 3 patients (nonreactors).

The initial periods of therapy with other drugs served as a basis for comparison. Cobra venom¶ in doses of 10 to 20 mouse units (1 to 2 cc) was injected into the deltoid muscle at least daily for periods ranging from three to seven days or until a therapeutic response was obtained. Clinical evaluation of the response and standardized exercise-tolerance studies were made at daily to weekly intervals throughout the period of study. Local pain, during and continuing for a short time after each injection, occurred almost uniformly. This prevented perfect control, since saline solution, which was used as a control injection, is not painful.

RESULTS

Effect on Exercise Tolerance and Pain

The intramuscular administration of cobra venom resulted in a 25 to 75 per cent increase in the standardized exercise tolerance in 7 of the 12 patients studied (Table 1), they included 3 of the 4 patients in Group 1, 1 of the 3 patients in Group 2 and 3 of the 5 patients in Group 3. In 6 of the 7 patients in

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§A mouse unit is the minimum lethal dose for a 20-gm mouse.

¶The cobra venom used in this study was supplied by Hynson, Westcott and Dunning Company, Baltimore, Maryland.

course of therapy as followed the first One patient
(Case 10) was benefited by the first course but did
not respond to the second or third course The

Toxic Effects
Local pain occurred in every case, even when the
drug had resulted in disappearance of the pain of

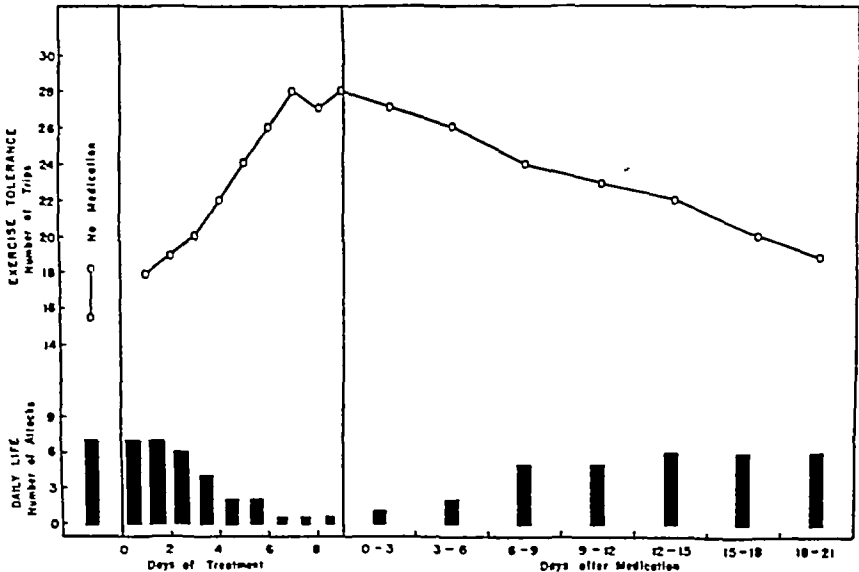


FIGURE 3 The Effect of Seven Injections of Cobra Ferom in Nine Days (average of observations in 5 patients)

reasons for this are not evident, this patient was
unresponsive to the usual medication employed in
angina pectoris In 2 patients a therapeutic response

angina pectoris, but in no case was this severe
enough to warrant discontinuation of therapy When
10 units was injected daily, no toxic effects were

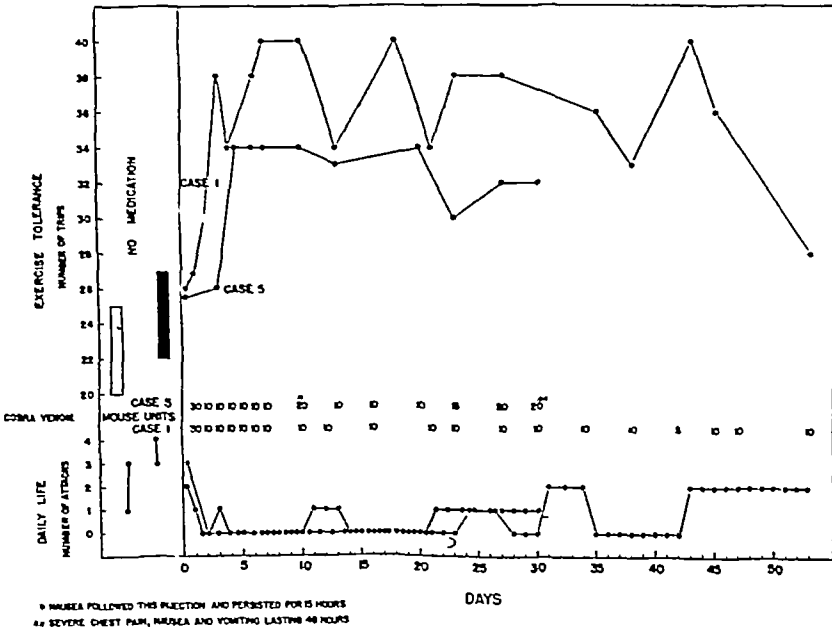


FIGURE 4 Time of Onset of the Effect of Cobra Ferom and the Result of Continued Therapy in Cases 1 and 5

was obtained with each course of therapy In 1 patient
(Case 8) the third course of therapy was less
effective than the first or second

observed in any patient One patient, who received
20 mouse units three times in twenty-four hours,
noted severe chest pain, nausea, vomiting and

absence of pain, the electrocardiogram following exercise was identical with that observed when the patient was receiving no medication and experienced pain on exertion (Fig 2)

Time of Onset of Effect

In 5 patients, seven injections of 10 mouse units each were given intramuscularly over a period of nine days—daily except Saturday and Sunday. The increase in exercise tolerance and decrease in daily attacks began about the fifth day, and the

weeks. One patient (Case 5) treated for four and a half weeks remained free from pain in daily life for three weeks and the increase in standardized exercise tolerance persisted. Because of the return of pain the dose was increased to 15 and then 20 mouse units (given twice), but further treatment had to be discontinued because of severe chest pain accompanied by nausea, vomiting and diarrhea. The other patient (Case 11); treated for seven and a half weeks, continued to be relatively free from pain in daily life for six weeks. In spite of con-

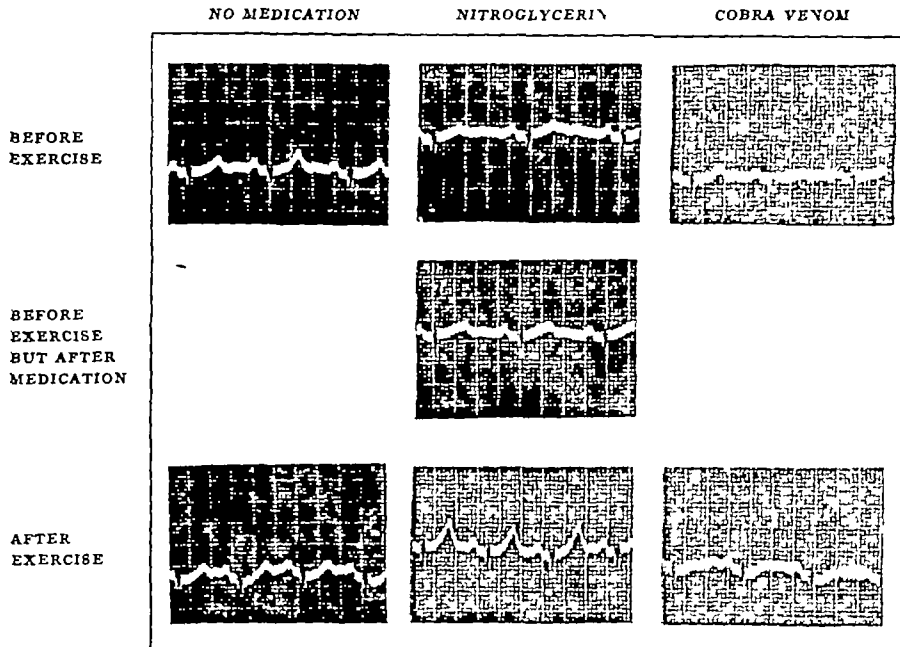


FIGURE 2 Electrocardiograms in Case 4

When no medication was administered, twenty trips over the two-step staircase caused pain and an average depression of the initial portion of the ST segment, as compared with the PR interval, of 1.3 mm. Two minutes after the sublingual administration of nitroglycerin, the same amount of work caused no pain and no change in the level of the initial portion of the ST segment. After six daily injections of cobra venom, the same amount of work caused no pain and an average ST segment depression of 1.4 mm.

maximum effect was observed in seven to nine days (Fig 3). In 6 patients, three injections of 10 mouse units each were administered the first day, followed by daily injections as noted above. In these cases the effect first became evident in three days, with a maximum effect on the fourth and fifth days. The results in 2 of these patients are illustrated in Figure 4. In 1 patient given 2 cc three times the first day severe toxic symptoms ensued and further therapy was impossible (see below).

Maintenance of Effect

In 5 cases injections of cobra venom were discontinued after a maximum effect was reached. Approximately six days later the pain returned during daily life and there was a measurable decrease in the standardized exercise tolerance (Fig 3). In 2 patients 10 units (1 cc) was injected semiweekly (Fig 4) and continued for four and a half to seven

weeks. One patient (Case 5) treated for four and a half weeks remained free from pain in daily life for three weeks and the increase in standardized exercise tolerance persisted.

Effect of Repeated Courses

In 5 cases, one and a half to eight weeks after the effect of the first course of therapy had disappeared, a second and in 4 of them a third course

TABLE 2 Effect of Repeated Courses of Therapy with Cobra Venom on the Standardized Exercise Tolerance

CASE No	NO MEDICATION	AFTER INJECTION OF COBRA VENOM FIRST COURSE	SECOND COURSE	THIRD COURSE
1	26	40	40	34
4	18	34	32	34
5	25	36	38	8
8	4	13	11	10
10	11	20	13	

of therapy (7 injections in nine days) was given (Table 2, Figs 1 and 4). In 4 of these cases essentially the same results were obtained by the second

MEDICAL PROGRESS

TUBERCULOSIS

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IN spite of four years of war and deprivation there has been, as yet, no indication of an anticipated and dreaded increase in tuberculosis mortality rates. On the contrary, the death rate has shown a gratifying decline. But, as Moriyama and Yerushalmy¹ point out, the danger has not yet passed.

Tuberculosis is a chronic disease and the current death rate is not a sufficiently sensitive index of changing conditions as they occur. The population may still be benefiting from the favorable rates of previous years, adverse conditions may have an accumulative effect that will be felt only in the future. In continental United States there was a decline of 1.2 per cent in the mortality rate of 1943 as compared with that of 1942. In Massachusetts, for the same period, however, the rate increased from 37.5 to 42.7 per 100,000 population, but the significance of this rise is not clear. The provisional 1944 death rate for the entire United States was 40.8, a decrease of 4.2 per cent from the rate for 1943.²

In Europe the situation regarding tuberculosis is extremely serious.³ A general increase in tuberculosis mortality has been noted since 1942. Great Britain, the Scandinavian countries and Switzerland have withstood the years of trial remarkably well, but in France, Belgium, the Netherlands, Germany, Austria, Czechoslovakia, Hungary, the Balkans, Italy and Poland the number of cases is increasing. Conditions are especially grave in the Netherlands, the Balkans, Italy and Poland.

MASS X-RAY SURVEYS

The photofluorogram or miniature x-ray film has become established as the most frequently used screening device for searching out tuberculosis in large groups of people. It is credited with being the principal factor for the low incidence of tuberculosis in the Army (judging from the annual hospital admission rate),⁴ and its application to case-finding is certain to become even more universal. In fact, Surgeon-General Thomas Parran⁵ has listed x-ray examination for the entire population first among the essentials of an effective tuberculosis-control program for the Nation.

On the basis of the extensive x-ray surveys that have been carried out the past few years by military and civil agencies, certain general statistical conclusions can now be reached. In New York City, for example, it is estimated that between 1933 and 1943 approximately 2,500,000 persons had chest

x-ray films taken for the purpose of discovering previously undetected disease and that about 2 per cent of these had evidence of chronic pulmonary tuberculosis.⁶ Approximately one third of these persons (0.6 per cent) were classified as having lesions of clinical significance, but further investigation usually demonstrates that about half of them (0.3 per cent) can eventually be considered arrested.

The statistics from other areas are quite comparable. In Canada, it has been found that the distribution of the disease is fairly uniform throughout the country, and that only 40 per cent of those who are diagnosed as having pulmonary tuberculosis are referred to sanatoriums for further study and treatment.⁷ In England, too, where miniature mass radiography has been used to detect unsuspected thoracic abnormalities, the London County Council reports the examination in one year of 45,682 persons, 112 of whom (0.2 per cent) were advised to accept hospital or sanatorium treatment.⁸

It has been estimated that within the past four years approximately 18,000,000 selectees and 3,000,000 industrial workers will have had chest roentgenograms for tuberculosis. The magnitude of the task — and the accomplishment — is just beginning to be realized as statistical data appear in the journals. From North Carolina, for example, Zanca and Herpel⁹ report a rejection rate of about 0.5 per cent for all types of tuberculosis in 100,000 consecutive selectees given chest photofluorograms. From Michigan, Kinzer¹⁰ analyzes the results on 105,141 selectees and finds that pulmonary tuberculosis was the cause for rejection in 999 (0.95 per cent). These figures are lower than the average, and they reflect creditably on the tuberculosis-control programs in those areas and on the local draft boards that weeded out manifest cases of tuberculosis before they reached the induction centers. For comparison it is well to cite the statistics of Gould,¹¹ who found that, in the chest x-ray films of 685,817 persons taken by the United States Public Health Service, reinfection tuberculosis was detected in 1.4 per cent. This figure is regarded as being representative of the general incidence of the disease as determined by mass fluorography.

Certain industries, all general hospitals and some institutions are especially fertile fields for x-ray surveys. "Industrialization," says Hilleboe,¹² "appears to be assuming a prominent role as a causal factor of high tuberculosis mortality rates." Of the more than a million workers examined by eight field units of the United States Public Health Service

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diarrhea, which disabled her and prevented further therapy. As noted above, similar symptoms occurred in a patient in whom the dose was increased from 10 to 20 mouse units (Fig 4).

COMMENT

It is evident from these studies that the administration of cobra venom to patients with angina pectoris is often followed by an increase in ability to work under standardized conditions and a corresponding improvement in daily life. This occurs in a fairly large proportion of patients, so that the results with cobra venom are in general comparable to those observed by us following any effective medication. It should be noted, however, that in the case of patients who respond markedly to the administration of nitroglycerin, cobra venom, although effective, is usually much less so. In one way the drug is more beneficial than other forms of therapy, for it may be helpful to Group 3 patients who are unresponsive to other types of medical therapy. It should be pointed out that the increase in exercise tolerance observed after the injection of cobra venom in some of these patients, although actually small, represents a large increase in ability to perform work.

There are, however, definite drawbacks to the use of the drug. Most important is the fact that it fails to have any effect on the underlying processes responsible for the discrepancy between the demands of the myocardium and the supply of blood. This is evidenced by the fact that the electrocardiogram after exercise is the same following cobra venom therapy as it is when no medication is given. Cobra venom apparently acts by preventing the patient from experiencing the sensation of pain. It is therefore comparable to the surgical procedures designed to interrupt sensory nervous pathways and should, we believe, be reserved for patients in whom surgery is contemplated but who may possibly avoid it by the use of this medication. It is, of course, worthy of a trial in patients with status anginosus due to any cause, but the delay before its effect becomes apparent limits its usefulness in the treatment of the pain of coronary failure or acute myocardial infarction.

The optimum results are obtained by administering 10 mouse units three times the first day, followed by one injection daily for seven days. As in the treatment of the pain of carcinoma and so forth, injections approximately twice a week must be continued. These doses do not result in untoward effect except for slight local pain. It is clear that

even with this regime escape from the effect of cobra venom occurs.

Another, although less important, drawback to the use of this drug is the cost of therapy. Furthermore, since the injections must be given daily for at least one week and semiweekly thereafter, cobra venom is not suitable to all ambulatory patients.

SUMMARY

The administration of cobra venom to patients with angina pectoris resulted in an increase in the standardized exercise tolerance and in clinical improvement in 7 of the 12 patients studied. This occurred in 4 out of 5 patients unresponsive to the usual medication employed in the treatment of angina pectoris.

The optimum method of administration was 10 mouse units (1 cc) three times the first day, followed by one injection daily for seven days, biweekly injections of 1 cc were then necessary to maintain the effect. If escape from the drug occurred, repetition of the initial course of therapy sometimes produced beneficial effects.

No untoward symptoms occurred with the dose recommended. Local pain invariably occurred, but in no case was it severe enough to warrant discontinuance of treatment.

Cobra venom does not prevent the electrocardiographic changes associated with exertion in patients with angina pectoris. Its action is therefore not that of coronary vasodilatation.

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refers only to the extent of the lesion as visualized on the x-ray film, and not to its degree of activity; the designation incompletely characterizes the lesion. From the standpoint of therapy and prognosis it is far more important to know whether the suspected area is active, inactive, arrested or healed. But it is precisely this point — the evaluation of the potential risk of progression — that is most difficult to determine in advance. A few criteria are, nevertheless, being gradually established.

In the first place, some impression of the stability or instability of a lesion can be gained from its appearance on the x-ray film. According to Reisner and Downes,²² the exudative lesion usually has ill-defined borders and is "soft" in appearance, the productive and fibrotic lesion is composed of discrete nodular densities or strand-like linear densities, the exudative-productive lesion is a combination of these two, and the fibrocalcific lesion usually consists of multiple, scattered, small, sharply defined, nodular densities. If the lesions are differentiated in this way, it is found that the risk of progression is far greater in the exudative or the exudative-productive group than it is in the other two. The risk is greatest in the first year but it extends beyond five years. The age of the patient or the presence of tubercle bacilli in the sputum at the time the lesion is discovered is less significant than the character of the lesion. The authors conclude: "It is necessary to regard all those exhibiting minimal lesions of a predominantly exudative character as of potential seriousness. It must also be emphasized that the intensive supervision of the case over extended periods of time is of the utmost importance."

Amberson²³ agrees that as much information as possible should be sought from the x-ray film, and even though one cannot pretend to interpret shadows in terms of exact pathology, the aim, at least, should be in that direction. He emphasizes, of course, that good visualization of a suspected lesion must be obtained before any attempt at interpretation can be made. In this connection it is worth while to remember that the anteroposterior lordotic projection may be a distinct aid in bringing out lesions that are hidden behind a clavicle in the routine, posteroanterior roentgenogram. The technique of obtaining this type of film is described in two brief and easily readable articles.^{25, 26}

The concept of prephthisical tuberculosis has been advanced by Mayer and Rappaport²⁷⁻³⁰ to clarify the diagnosis and treatment of early lesions. The term "prephthisical tuberculosis," according to the authors, is applied to all tuberculous lesions in the chest that precede the development of chronic pulmonary tuberculosis or phthisis. In addition to those with persistent but stable x-ray lesions, prephthisical tuberculosis includes those who have recently acquired tuberculin sensitiveness and those who have had a recent episode of simple pleurist

with effusion. Mayer and Rappaport contend that it requires observation to determine whether a given lesion is in a phthisical or prephthisical stage. Every tuberculous lesion must be assumed phthisical until proved otherwise. But, to treat all tuberculous lesions as if they were phthisical is wrong because the majority of them show spontaneous arrest and healing. It is argued, furthermore, that young persons with recently acquired prephthisical lesions should not be exposed to contact with open phthisis in tuberculous wards until observation has proved the diagnosis and laboratory tests have demonstrated the contagiousness of their disease. They conclude "Immediate treatment is most important in phthisical lesions. Prolonged observation with frequent x-raying is most important in prephthisical lesions."

Amberson's³¹ viewpoint is not wholly in agreement with this. He admits the difficulty in distinguishing lesions that threaten to advance and must be treated from those that spontaneously become arrested without any enforced alteration in the patient's mode of life. But it is not enough to glance at an x-ray film and decide what adjustments the patient should make. All identifiable factors must be considered in the evaluation of a given case. Amberson recommends that patients with minimal lesions be hospitalized for about ten days to allow for an intensive work-up of their cases. Since the rate of evolution of unstable lesions, particularly in young people, is extremely variable, observation in a hospital is a definite necessity until the trend is determined and effective treatment is established. To take the point of view that these patients need nothing more than periodic x-ray examination, that most of these infiltrates will heal without treatment and that treatment is not necessary until they have undergone necrotic changes is unwarranted. The time to start effective treatment, according to Amberson, is before the phase of advanced tuberculosis has asserted itself. Treatment should be individualized, but for the young person, prescribed bed rest usually varies from three months to a year. Thereafter graduated exercise is begun, and regulation of the patient's daily life should continue for the next year or two.

The presence or absence of tubercle bacilli in the patient's sputum or gastric contents may be an uncertain guide in the evaluation of his clinical status. If the sputum is negative by culture or guinea-pig inoculation, — negative stained smears are worthless in such cases, — gastric specimens should always be obtained whenever there is a suspicious roentgenologic lesion. Feld³² has shown that the person with a negative sputum culture but with a positive gastric test is not entirely innocuous. Some of these patients eventually develop positive sputums. He recommends treating a patient with a positive gastric content exactly like a positive sputum case. At the Muirdale

from 1942 to 1944, about 15 per cent had x-ray evidence of reinfection-type tuberculosis. It is planned, soon, to send twenty such x-ray units to local communities, at the request of state health departments, and to assist states and cities in starting mass x-ray surveys among industrial workers and among the 15,000,000 persons admitted each year to general hospitals.¹³

General hospitals are still not utilizing routine chest roentgenography to the extent that seems advisable, and this point is stressed in a number of recent articles. Small film roentgenography, as a matter of fact, is admirably suited to case-finding in general hospitals, since there is no expense entailed in assembling people for the study and the films may be interpreted by staff roentgenologists. Besides, in general hospitals, facilities already exist for completing clinical examinations and providing ambulatory care.^{12, 14}

"Miniature chest radiography," say Scatchard and Duszynski,¹⁵ "can no longer be called experimental." Then they add significantly "It is now possible to x-ray every admission to all general hospitals as part of the routine. The small film of the chest provides an excellent case-finding method, as well as an extremely valuable diagnostic procedure." Of 3000 consecutive x-ray examinations made by these investigators, significant thoracic lesions were noted in 1070 (35.7 per cent). Of 1832 patients admitted to the hospital, 36 unsuspected cases of tuberculosis were discovered. Wilson¹⁶ has also commented on the indispensability of the x-ray for the early diagnosis of chest lesions—before they reach a hopeless, advanced stage. Mattison,¹⁷ too, believes that case finding among symptomatic persons or contacts is either entirely inadequate or too limited in scope to discover an appreciable number of patients in the minimal stage of tuberculosis. Mass roentgenography, he suggests, provides a method for reducing the time interval between the onset of the disease and the discovery of its presence.

If additional evidence were needed to prove this point, the work of Bloch and Tucker¹⁸ at the clinics of the University of Chicago could be cited. Their study of 15,000 patients whose chests were fluoroscoped regardless of their complaints revealed a tuberculosis incidence of 1.4 per cent, and on this basis, it is estimated that 600,000 persons with active tuberculosis will come under medical care this year—without the underlying disease being suspected.

In addition to the general hospitals, case-finding is also profitable among the inmates and employees of institutions for the care of those with chronic diseases. Tuberculosis sanatoriums themselves are not entirely blameless as a source of new cases, and they may, in a way, be a reservoir rather than a trap for the disease. Myers¹⁹ acknowledges the need of a place for the isolation of every contagious

case of tuberculosis, but he goes on to say "Our sanatoriums have removed from homes and communities many contagious cases, but they have created a serious problem by spreading tubercle bacilli from patient to patient, to personnel and to visitors. Only recently has any worthwhile attention been paid to the protection of others against the tubercle bacilli of institutionalized patients."

There can be no question that the personnel of some tuberculosis sanatoriums are often inadequately protected against the disease. Tuberculin testing and frequently repeated x-ray examinations of sanatorium staff members are essential for the prompt discovery of infected persons. In this respect the program of employee care furnished by the Cheshire Joint Sanatorium in England is commendable.²⁰ There, each new member of the personnel is given a physical examination, a tuberculin test and a chest x-ray examination, and in addition, the erythrocytic sedimentation rate is determined. Those with positive Mantoux reactions are re-examined semiannually. Those with negative ones are re-tested at monthly intervals, and special care is taken to provide them with proper guidance and treatment if the Mantoux test becomes positive.

In mental hospitals, where the incidence of pulmonary tuberculosis is high and where there has been a grave, wartime reduction in personnel, the problem of tuberculosis control is especially serious. In Oklahoma, for example, the incidence of tuberculosis in the mental hospitals is ten times greater than among the general population.²¹ As a matter of fact, 7 per cent of all the state's tuberculosis deaths in 1943 were traceable to mental hospitals. In New York State, the average annual tuberculosis death rate in 1939-1941 was 593.6 per 100,000 for the mentally ill, whereas it was only 46.8 for the state as a whole.²² The patient population in the mental institutions of the state was only 0.6 per cent of the total population, but it accounted for 8.1 per cent of all tuberculosis deaths.

It is no wonder then that employees in mental hospitals show a greater incidence of tuberculosis than those employed in other occupations. Among the 14,228 employees in twenty New York mental institutions, 156 (1.1 per cent) showed x-ray evidence of clinically significant tuberculosis, an incidence that is almost twice as great as that of workers in general industrial occupations. Surprisingly, x-ray examination of 5735 applicants for institutional employment revealed also that 61 (1.1 per cent) had significant pulmonary tuberculosis. This high figure, which is twice that of the general population, is a reflection of the low economic level of the applicants for work in mental hospitals.

THE SO-CALLED "EARLY" LESION

Thanks to mass x-ray surveys, the majority of tuberculosis cases that are being discovered are in the minimal stage. Since the term "minimal"

Sanatorium it is current practice to keep such suspicious cases for eight weeks, during which time intensive laboratory studies are carried out. At the end of this period, a patient may be discharged, if examination warrants it, with the diagnosis "no clinical evidence of active tuberculosis." Medlar and Reid,³³ on the other hand, believe that patients can be classed as "pathologically active, clinically inactive" when the lesion shows no evidence of progression and yet tubercle bacilli can be detected in the sputum by culture or guinea-pig inoculation. These investigators performed sputum and gastric examinations on 252 employees in the Home Office of the Metropolitan Life Insurance Company. They found tubercle bacilli in 66 persons, 63 of whom either had clinically active tuberculosis at the time of the examination or had had sanatorium treatment for active tuberculosis in the past. Judging from their statistics, those with a minimal disease have as difficult a time in eradicating tubercle bacilli as do those with moderately advanced disease. They conclude, "The demonstration of tubercle bacilli in ex-sanatorium patients at work simply stresses the chronicity of a tuberculous infection regardless of the extent of the disease."

CHEMOTHERAPY AND ANTIBIOTICS

No chemical agent has yet been discovered that is effective, safe and acceptable for general use in the treatment of clinical tuberculosis. Great interest— from an experimental standpoint — continues to center on the sulfones, especially promin (sodium *p,p'*-diaminodiphenylsulfone-*N,N'*-dioxetose sulfonate) and diasone (disodium formaldehyde sulfonate, 4,4'-diamino diphenylsulfone).

Research during the past five years has demonstrated that promin has a marked deterrent action on tuberculosis in guinea pigs, that it can bring about resolution of some experimental tuberculous lesions already established and that it can lengthen the survival time of infected animals. Logically, therefore, it could be assumed that, by the inoculation of guinea pigs with virulent tubercle bacilli, and by allowing the bacilli to disseminate and multiply before initiating chemotherapy with promin, it might be possible to stimulate the natural immunogenic processes of the animals. Such an experiment could be regarded as being analogous to vaccination with whole bacilli—with this difference, that chemical attenuation of the micro-organisms might be accomplished *in vivo* after inoculation. This hypothesis has been tested recently by Feldman and Hinshaw,³⁴ but no experimental evidence was found to substantiate it. Infected animals treated with promin and subsequently reinfected showed no significant modification of their disease as compared with control groups. Promin was found to be tuberculostatic, or suppressive, in its action, not tuberculocidal. Nevertheless, the

authors believe that a drug that "serves only a suppressive function does not speak against its practical therapeutic efficacy," and they call attention to the therapeutically valuable but merely suppressive roles of quinine and atabrine in malaria. Clinical studies with promin-mist inhalations have been continued by Edlin and his co-workers.³⁵ The technic for the administration of these mists is still being perfected, and only a small number of cases have been investigated. Twenty-four patients were given promin inhalations (a 40 per cent solution at pH 5.6-6.0) in divided doses up to 3.0 gm daily, for a total average dose of about 200 gm. Cyanosis appeared in 23 of these cases, and anemia in 12. There was some evidence that these inhalations were of benefit in cases of endobronchial ulceration, but its value in the therapy of parenchymal disease was questionable.

The role of diasone as a therapeutic agent is also unsettled. According to the late Dr. Kaziss and his colleagues³⁶ diasone is less toxic for mice, rats and rabbits than most of the well known sulfonamides and far less toxic than diaminodiphenylsulfone. On the other hand, diasone appears to be appreciably more toxic for human beings. One death attributed to diasone has already been reported,³⁷ and two other fatalities have occurred during the course of diasone therapy.³⁸ Skin lesions, especially, must be regarded as potentially serious and warrant immediate discontinuation of the drug.

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Because the sulfones have proved themselves either too toxic or too indecisive in their action, attention is turning from them toward the antibiotics. Penicillin, the most important member of this class of substances, is without effect in tuberculous, but it may be an aid in the treatment of mixed (tuberculous and pyogenic) empyemas. Hirschfeld and his co-workers⁴² cite the case of a patient with bilateral pulmonary tuberculosis in whom a pyogenic empyema developed following an intrapleural pneumonolysis. Penicillin, administered

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Medlar and Reid,³² on the other hand, believe that patients can be classed as "pathologically active, clinically inactive" when the lesion shows no evidence of progression and yet tubercle bacilli can be detected in the sputum by culture or guinea-pig inoculation. These investigators performed sputum and gastric examinations on 252 employees in the Home Office of the Metropolitan Life Insurance Company. They found tubercle bacilli in 66 persons, 63 of whom either had clinically active tuberculosis at the time of the examination or had had sanatorium treatment for active tuberculosis in the past. Judging from their statistics, those with a minimal disease have as difficult a time in eradicating tubercle bacilli as do those with moderately advanced disease. They conclude, "The demonstration of tubercle bacilli in ex-sanatorium patients at work simply stresses the chronicity of a tuberculous infection regardless of the extent of the disease."

CHEMOTHERAPY AND ANTIBIOTICS

No chemical agent has yet been discovered that is effective, safe and acceptable for general use in the treatment of clinical tuberculosis. Great interest — from an experimental standpoint — continues to center on the sulfones, especially promin (sodium *p,p'*-diaminodiphenylsulfone-*N,N'*-didextrose sulfonate) and diasone (disodium formaldehyde sulfoxylate, 4,4'-diamino diphenylsulfone).

Research during the past five years has demonstrated that promin has a marked deterrent action on tuberculosis in guinea pigs, that it can bring about resolution of some experimental tuberculous lesions already established and that it can lengthen the survival time of infected animals. Logically, therefore, it could be assumed that, by the inoculation of guinea pigs with virulent tubercle bacilli, and by allowing the bacilli to disseminate and multiply before initiating chemotherapy with promin, it might be possible to stimulate the natural immunogenic processes of the animals. Such an experiment could be regarded as being analogous to vaccination with whole bacilli — with this difference, that chemical attenuation of the micro-organisms might be accomplished *in vivo* after inoculation.

This hypothesis has been tested recently by Feldman and Hinshaw,³³ but no experimental evidence was found to substantiate it. Infected animals treated with promin and subsequently reinfected showed no significant modification of their disease as compared with control groups. Promin was found to be tuberculostatic, or suppressive, in its action, not tuberculocidal. Nevertheless, the

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ministered intravenously and intrapleurally, kept the empyema in check, permitted the completion of a thoracoplasty and enabled the patient to be discharged to her home. A similar experience with penicillin in mixed empyemas following pneumothorax is reported by Howlett and Lester.⁴¹ Penicillin, prophylactically, can also be used with reasonable success in the preoperative and postoperative periods in cases of lobectomy and pneumonectomy as a means of preventing empyema.⁴²

So new is the discovery of tuberculocidal antibiotics that research on practically all of them is still in the experimental stage. The one noteworthy exception is streptomycin, isolated from *Actinomyces griseus* by Waksman and his group⁴³⁻⁴⁵ at the New Jersey Agricultural Station. Streptomycin is similar to another related antibiotic, streptothricin, in its bactericidal activity against gram-negative bacteria, its low toxicity and in its in-vitro inhibition of tubercle bacilli.^{45, 46} Streptomycin is the first of the newer antibiotics whose toxicity is so low and its in-vitro tuberculocidal activity so definite as to warrant testing in guinea pigs. In these animals its action is comparable to that observed with the sulfones, — its tuberculosissuppressive effect is "striking," — and most encouragingly, it appears to be well tolerated.⁴⁷ Reports on the effect of streptomycin on human tuberculosis have not yet appeared, but clinical trials on 22 patients have been under way since December, 1944.⁴⁸

Other antibiotics that are believed to possess antituberculosis activity are being discovered at so rapid a rate that it is only possible to make brief mention of them. Asheshov and Strelitz⁴⁹ have obtained a tuberculocidal product from the fungus *Aspergillus fumigatus*, and in-vitro tests show that even impure preparations are active in dilutions up to 1,500,000.⁵⁰ Gerber and Gross⁵¹ and Kurung⁵² have also reported inhibition of the growth of tubercle bacilli by presumably other products from molds belonging to the family Aspergillaceae. Other investigators⁵³ have found that buttercup juice stops the in-vitro growth of human tubercle bacilli, but the toxicity of the juice for laboratory animals is so great that therapeutic tests have been impossible.

MISCELLANEOUS TOPICS

Bacteriology When tubercle bacilli are inoculated into the chorioallantoic membrane of a chick embryo, they grow rapidly and the character of the lesion that results varies somewhat with the type and virulence of the injected bacillus. It had been hoped that chorioallantoic-membrane cultures could be used for testing grades of virulence. Fite and Olson⁵⁴ inoculated forty-six different strains of acid-fast bacilli into chick embryos and concluded from these tests that organisms of high virulence grew most rapidly and that avian and bovine

tubercle bacilli produced characteristic lesions. Unfortunately, however, the chorioallantoic membrane varies too widely in response to avirulent acid-fast bacilli to make the procedure, by itself, of value in determining the virulence of a given strain or its species.

Emmart and Seibert⁵⁵ have taken advantage of the chick embryo to test the tuberculostatic action of various serum fractions obtained from normal, "sensitized" and tuberculous rabbits. Serum from tuberculous rabbits and from those sensitized with a purified tuberculo-protein preparation possessed tuberculostatic activity, as determined by the size and development of tubercles on the chick embryo. Pooled serums of patients with minimal tuberculosis contained a gamma globulin that also seemed to possess a tuberculostatic effect, although the data according to these investigators, "were insufficient to be statistically significant."

The problem of the morphology of tubercle bacilli, especially the question whether they exist in forms other than acid-fast rods, is still unsettled, but the work of Alexander-Jackson⁵⁶ during the past ten years has brought forth considerable evidence to support the hypothesis that globoid and coccoid nonacid-fast forms do exist. These are described as a "zoogloal plasmodium consisting of granules or larger globoid bodies surrounded or enmeshed by amorphous material." These zoogloal forms can be seen in unstained material or by special staining technics.⁵⁷ Photographs taken with the electron microscope indicate that they are able to revert to rod forms, and vice versa. Minute, virus-like tubercle bacilli, on the other hand, probably do not exist. According to the researches of Soltys and Taylor,⁵⁸ tubercle bacilli are retained by Gradocol membranes of known pore diameter that allow ready passage of the ultraviable viruses.

Within the past few years the technic of fluorescence microscopy has improved to such an extent that the method can now be regarded as being available for routine laboratory use in the detection of tubercle bacilli in sputum or other excretions. Lempert,⁵⁹ in an excellent review, discusses the principles underlying fluorescence microscopy, as well as the practical, laboratory setup. In comparing this method with the Ziehl-Neelsen staining technic on three hundred specimens, Lempert finds the former is faster and at least equally as accurate as the latter. In addition it is neither expensive nor difficult. Voigt⁶⁰ prefers the luminescence technic, since a greater number of organisms can be detected in sputums by this method than by the usual staining methods. In tissue sections, too, Tanner⁶¹ finds more organisms by fluorescent staining than by using the regular fuchsin stain. Curiously, neither method appears capable of staining all the organisms in a given field. Tanner believes that there may be additional organisms that are never stained by any of the present methods.

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Vaccines and serums In spite of some recent evidence favoring their use, the status of vaccines for the prevention of tuberculosis is still questionable. A report from Brazil on the work with BCG immunization in children from 1927 to 1944 includes some data on 161,152 immunized children and an additional 3000 anallergic persons in other age groups.⁷¹ Although the technic of immunization and the immediate response to inoculation are described, no conclusions are given concerning the prophylactic value of the method.

The data from Chicago are more specific on this point. There, under the direction of the staff of the Municipal Sanitarium, a ten-year study of BCG prophylaxis involving 2515 children has been conducted.⁷² In 1204 vaccinated children in whom no source of contact with tuberculosis was known, there were 3 cases of tuberculosis and 1 death from the disease. On the other hand, in 1213 unvaccinated controls, there were 23 cases of tuberculosis and 4 deaths. Similarly, in 98 vaccinated newborn infants with known contact to tuberculosis, only 1 developed the disease and there were no deaths, whereas in the unvaccinated group of 63 cases, 4 children developed tuberculosis and 3 died. Considering the groups as a whole, there were 27 cases of tuberculosis and 7 deaths in the unvaccinated group as compared with 4 cases and 1 death in the vaccinated. These studies indicate that BCG may have a definite prophylactic value, especially in the early years of life.

Vaccination may also prove worthwhile in special groups of the adult population, such as inmates of hospitals for the insane. At the Mental Hospital in Kingston, Jamaica, for example, tuberculosis causes 25 per cent of all deaths and 86 per cent of those with clinical tuberculosis develop the disease while in the institution. In this tuberculosis-ridden population, Wells and his co-workers⁷³ have been experimenting for more than ten years with a heat-killed vaccine. They found that both the attack and death rates for tuberculosis were significantly lower among recipients of the vaccine administered intracutaneously than among persons alternately chosen but not vaccinated, who served as controls. It was observed, too, that those persons who had a positive tuberculin test on admission also had lower attack and death rates than those with weak or negative reactions, vaccinated persons and the controls. The suggestion is advanced that vaccination may be of value in other groups that are exposed to an unusual risk of tuberculous infection, such as medical students, nurses, attendants and contacts.

In a recent paper, Chadwick⁷⁴ makes mention of the investigations of Dr. Cleveland Floyd on "fractions of the tubercle bacilli that have not been used before in treatment." The fraction that is currently being studied is said to prevent the development of the disease when injected into

previously infected animals. Early results on a few patients are regarded as encouraging, but no definite report has as yet been made. The Boston Tuberculosis Association has taken an active interest in this work and is making efforts to obtain the financial support that the project deserves.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31421

PRESENTATION OF CASE

A thirty-seven-year-old woman entered the hospital complaining of diarrhea.

Eleven years previous to admission she had her first attack of diarrhea, with several liquid stools daily, without blood, pus or mucus. She was nauseated and had periumbilical cramps, which were relieved by evacuation. The first episode lasted about six weeks. A year later, and again four years later, she suffered similar attacks of diarrhea. Following her third acute episode, she had about three semiformed stools daily, without abdominal cramps or weight loss. Nine weeks before admission diarrhea recurred, with as many as ten watery stools daily. Nausea and cramps were present. A lemon-sized mass was noted in the right lower quadrant, at times it became enlarged and then decreased in size spontaneously, with audible gurgles. Five weeks before admission, because of persistence of the above symptoms, and because a barium enema had shown an obstruction in the region of the cecum, an ileocolostomy was done at another hospital. Two weeks later the mass in the right lower quadrant, which had continued to increase in size after the operation, ruptured through the upper end of the incision and began to discharge small-bowel contents.

The patient was markedly emaciated, pale and dehydrated. Examination of the heart and lungs was negative. The abdomen showed a fistula at the upper end of a lower right rectus incision.

The blood pressure was 110 systolic, 70 diastolic. Examination of the blood showed 8 gm. of hemoglobin and a white-cell count of 7200, with 70 per cent neutrophils. The red cells showed considerable achromia, with moderate variation in size and shape. The urine was normal. The nonprotein nitrogen was normal. The total serum protein was 4.4 gm. per 100 cc., and the chloride 94 milliequiv. per liter. A barium enema passed only to the hepatic flexure (Fig. 1), beyond which point the patient could not tolerate the enema. No fistula was evident. No true shelf was seen at the end of the barium column. A Miller-Abbott tube was

inserted, and on fluoroscopy was found to have descended to the cecum. Barium was then introduced into the bowel through it. The ascending colon was normal, but the barium did not pass the region of the hepatic flexure. The point of entry of the fistula into the bowel was not demonstrated. Although it seemed shrunken, the cecum filled with barium and the ileocecal valve opened. An-



FIGURE 1 Roentgenogram of Bowel following a Barium Enema

Note the abnormal haustra and the obstruction in the region of the hepatic flexure.

other barium enema was given. The normal haustra of the colon were not evident, and the colon seemed to be somewhat shortened. There was no definite rigidity of the wall, and no ulcerations or granulations could be seen. Barium did not pass the hepatic flexure. When the colon had emptied, long areas of segmentation were seen (Fig. 2).

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. EARLE M. CHAPMAN: It seems fairly clear that some process was causing obstruction, probably in the region of the hepatic flexure. The lemon-sized mass was the dilated cecum resulting from the low-grade obstruction. When that went down everything subsided, but this had been going on for many years. Finally an ileocolostomy was done at another hospital, which, I assume, was an error.

because it joined the bowel to the cecum just below the point of obstruction and nothing was accomplished

May we see the x-ray films?

DR MILFORD D SCHULZ The chest film shows evidence of an old tuberculous lesion in the right apex. On this film, taken at the time of the first barium enema, one can see that the bowel is short-



FIGURE 2 Roentgenogram of Bowel following a Barium Enema

Note the segmentation of the bowel

ened and has no normal haustra. No barium passed beyond the hepatic flexure. On the second examination, similar observations were found and one can see a curious segmented appearance when the bowel had emptied.

DR CHAPMAN Do you attribute any particular significance to the segmentation?

DR SCHULZ It is an abnormal appearance, somewhat similar to what is seen in an unused bowel, although here one wonders about colitis. There are no definite ulcerations. If it is colitis, it is of long standing with scarring. The cecum does not seem to be definitely abnormal. Barium was introduced through a Miller-Abbott tube, but there is no apparent fistula and the barium does not go beyond this point, which is in the region of the hepatic flexure. The cecum itself does not look definitely abnormal.

DR CHAPMAN Is that the normal pattern of

contraction of the cecum? The contraction of an empty bowel on a small bolus.

DR SCHULZ It may be quite normal. I do not believe that the colon as a whole is normal, I can see no evidence of a fistula in these films nor of a short circuit.

DR JACOB LERMAN What was the operation? Did they do a cecostomy or a transverse anastomosis?

DR CHAPMAN Presumably it was a junction of the ileum and the cecum, and they closed her up tight. The wound broke open, and Nature took care of things, performing a spontaneous ileostomy, that is, if I interpret these findings properly. Am I correct, Dr. Castleman?

DR BENJAMIN CASTLEMAN Yes.

DR CHAPMAN Dr. Schulz, you are not going to give us any diagnosis on the basis of your observation?

DR SCHULZ One is only justified in saying that the patient had an obstructing lesion in the hepatic flexure, the nature of which is not determined. The colon is abnormal, there was probably a colitis.

DR CHAPMAN There is no evidence of an active lesion in the lungs?

DR SCHULZ I do not believe that the lesion is active.

DR CHAPMAN To come to the point, one has to decide what was the process at the point of obstruction in the large bowel in this woman of thirty-seven. The procedure is to review the causes of chronic intermittent diarrhea and to list them in the order of likelihood.

Now that I have seen the chest film, with the x-ray evidence of tuberculosis at the apex, my first choice is tuberculous infection. The chance that this woman had a tuberculous mesenteric adenitis following the lesion in the chest when she was in her early twenties, which subsequently caused a cicatrizing scar in this region, is good. There is no possible way from the evidence at hand to prove this diagnosis.

Another thing that we must think of is that there were adhesions, not due to infection but to some mechanical process that had gone on previously. There is no history of a previous operation for appendicitis. Was there a scar of an appendectomy in the right lower quadrant?

DR CASTLEMAN It is not mentioned in the record.

DR CHAPMAN The appendix has not been described in these films.

I am reminded of the history of the case of a fifty-two-year-old man who recently came in because of intestinal obstruction, with a mass in the right lower quadrant. Of course, we thought that it was probably a tumor. When he was explored, the operator found a cicatricial band from an old appendectomy entirely encircling the cecum. He made a complete recovery.

When we think of some of the physiologic causes of chronic intermittent diarrhea in young women, one of these is gastrogenic in origin, resulting from a low hydrochloric acid in the stomach, but that is entirely unlikely with this picture. Endometriosis can do queer things. It is said that 10 to 20 per cent of all women between the ages of thirty and the menopause have some degree of endometriosis, these implants frequently land on the sigmoid, in the rectal region or low in the pelvis. The hepatic flexure is a rather unlikely location for an endometrial implant. This is the first case of a woman that I have discussed at a clinicopathological conference in which the record has failed to mention the catamenia. Were the attacks of obstructing pain coincidental with menstruation?

DR CASTLEMAN: Apparently not.

DR CHAPMAN: There are other sorts of physiologic abnormalities that can explain these symptoms, such as pancreatic disease. With some abnormality in pancreatic function she could have had a sprue-like disease, but I hardly see how it could have caused an obstruction at the hepatic flexure.

How about congenital disorders? She was quite well advanced in years to have had a congenital disorder. Of course, a Meckel's diverticulum might have caused it in some way, or a volvulus or some sort of queer bands of adhesions in the intestine. All these seem unlikely. Can Dr Schulz rule out intussusception in these films?

DR SCHULZ: There is nothing to indicate intussusception.

DR CHAPMAN: Then we come to the last one in the series that we have to consider, that is, a new growth of some type. New growths are not so common in this region as in the sigmoid and rectum, nor do I believe that carcinoma of any type could have been present for eleven years. The patient was relatively young, thirty-seven years, and the picture she presented does not favor malignant disease, it is just the picture of a patient with poor nutrition due to chronic, intermittent, large-bowel obstruction.

Now that I have gone through all these possibilities, I am going to return to my first choice. I believe that this woman, who had tuberculosis in the right apex at the age of twenty, probably had a small area of tuberculosis somewhere in the abdomen that had become adherent to the serosal surface. A tuberculous lesion there could gradually contract through the years and finally cause obstruction.

I have not even mentioned ulcerative colitis, because I do not believe that the patient had this disease. The x-ray appearance is not that of ulcerative colitis. Dr Schulz says it is the appearance of an unused bowel.

DR SCHULZ: I do not believe that one can rule out ulcerative colitis on this appearance.

DR JOSEPH C. AUB: How about regional ileitis?

DR CHAPMAN: I did not mention it because I do not believe that this disease was in the ileum. We must accept the fact that the obstruction was in the cecum.

DR AUB: I agree.

DR SCHULZ: It was in the cecum or above the cecum.

DR CHAPMAN: In the hepatic flexure.

A PHYSICIAN: Was a guaiac test done on the stool?

DR CASTLEMAN: I think that it was positive.

CLINICAL DIAGNOSES

Chronic ulcerative colitis, with adenocarcinoma of hepatic flexure.

DR CHAPMAN'S DIAGNOSES

Pulmonary tuberculosis, old.

Tuberculous colitis.

Intestinal obstruction from tuberculous scars and adhesions.

ANATOMICAL DIAGNOSES

Chronic ulcerative colitis.

Adenocarcinoma of hepatic flexure.

PATHOLOGICAL DISCUSSION

DR CASTLEMAN: Dr McKittrick operated on this patient and found so many adhesions in the right lower quadrant that he was unable to decide what had been done at the earlier operation. He thought that the entire bowel was abnormally thickened. The serosa over the bowel was thickened, and he believed that this was probably due to ulcerative colitis. In the region of the obstruction, he felt a large mass in the bowel, which appeared to be a carcinoma. He therefore performed a transverse ileocolostomy as the first stage for relieving the obstructing lesion.

The patient went home and came back later, at which time he removed the right colon including the hepatic flexure. The obstruction proved to be a completely annular adenocarcinoma, there were no metastases to the regional nodes, although the surrounding lymphatic vessels over the tumor in the wall of the bowel were involved with tumor. The rest of the bowel that he resected showed chronic ulcerative colitis. There were numerous healed ulcers with pseudopolyps of mucosa, such as one sees in the characteristic form of ulcerative colitis. So this was a case of chronic ulcerative colitis on top of which an adenocarcinoma had developed.

CASE 31422

PRESENTATION OF CASE

First admission. A twenty-three-year-old man entered the hospital complaining of diarrhea.

Eleven years previous to admission he had suffered from an acute attack of colitis caused by a

Flexner dysentery bacillus He was bedridden for about six months, and at the end of that period his stool cultures became negative. During the next two years he had had bloody, mucoid stools, often as many as twelve daily. The number had slowly decreased, and on entry he was having about four a day. During the three years before admission there had been no blood or mucus in the stools. At one time his weight was 50 pounds, but this had gradually increased to an admission weight of 130. He had frequently had slow-healing ulcers on the legs.

Physical examination revealed a pale, poorly nourished man. The fingers and toes showed slight clubbing. There was slight tenderness in the right upper quadrant of the abdomen on deep inspiration.

The temperature was 98.6°F, the pulse 80, and the respirations 20. The blood pressure was 110 systolic, 70 diastolic.

Examination of the blood revealed a white-cell count of 6600, with 75 per cent neutrophils, and 12 gm of hemoglobin. The urine was normal. A blood Hinton test was negative. The stool was fluid, light brown, neutral in reaction, negative for mucus and gross blood but strongly guaiac positive, no parasites were found on repeated examinations. A barium enema revealed saw-tooth irregularities of the colon throughout its course, including the cecum. There was marked granularity of the mucosa. No filling defects were seen, and the colon was not tender. The ileocecal valve was narrowed and rigid for a distance of 3 to 4 cm, proximal to this the terminal ileum did not appear unusual. The liver was enlarged and overlaid the right iliac crest. Proctoscopic examination showed an edematous, thickened, red and roughened mucosa. In the lower sigmoid was a red, partly ulcerated area occupying about half the circumference of the bowel and composed of a number of polypoid nodules. The bowel wall at this site was flexible.

The patient was discharged on a high-vitamin, low-residue diet, with supplementary vitamins and iron.

Second admission (one year later) The patient was readmitted for study. He had been leading a regular, quiet life and had been having about five stools daily.

Physical examination revealed marked clubbing of the fingers and toes.

Examination of the blood revealed a hemoglobin of 10.5 gm. The stools gave a +++ guaiac reaction. A barium enema passed slowly but steadily from the rectum to the cecum, instead of in the usual segmental manner. There was some shortening of the colon, with several areas of moderate narrowing. There were multiple ulcerations throughout the entire colon. The ileocecal valve appeared thickened. Definite ulceration was seen in the distal 10 cm of the ileum. Sigmoidoscopy revealed a narrow lumen and a stiff bowel wall. The mucosa

was irregular and granular with fibrotic elevations 1 to 2 mm in height. One area in the sigmoid was dark brown.

The patient was discharged on 5 gm of sulfathalidine daily.

Third admission (six months later) The patient's condition had remained essentially unchanged. Sulfathalidine was discontinued one week before admission. The stools had been loose, yellow and often watery. His weight was 138 pounds, which he considered normal.

On admission a stool specimen was liquid and tan and gave a + guaiac reaction. The red-cell count was 3,120,000, and the hemoglobin 57 gm.

He was discharged on sulfathalidine.

Final admission (eighteen months later) Four weeks before admission the patient, who was then twenty-six years old, had experienced an increase in the number of stools to 6 daily, with cramps just before evacuation and blood in the stools. He had been working hard and tired easily. He began to lose weight. Two weeks later he noted the onset of severe pain in the right upper quadrant and right flank, it was not colicky and was intermittent. A day or two later a pain like a "muscle stitch" appeared in the left upper quadrant. Both pains disappeared spontaneously ten days before admission, leaving no residue. He had had no fever, nausea or vomiting.

Physical examination showed evidence of recent weight loss and a haggard appearance. The tongue was bright red at the tip and edges, with some loss of papillae. The heart and lungs were normal. A superficial, lobulated, firm, nontender mass was felt in the right upper quadrant. It extended into the right lower quadrant and was palpable in the right costovertebral angle. It was fixed to lateral motion but descended on inspiration. Peristalsis was active. Many external hemorrhoids were found. The right leg and thigh were somewhat greater in circumference than those on the left. The reflexes were physiologic.

The temperature was 98.6°F, the pulse 90, and the respirations 20. The blood pressure was 120 systolic, 80 diastolic.

Examination of the blood revealed a hemoglobin of 11.6 gm and a white-cell count of 10,300, with 58 per cent neutrophils. A blood Hinton reaction was negative. The urine was normal. Stool specimens were dark brown and guaiac negative. The prothrombin time was 30 seconds (normal, 18 to 20 seconds). The nonprotein nitrogen was 22 mg per 100 cc, the total protein 6.3 gm, and the chloride 105 milliequiv per liter.

The abdomen became distended, but peristalsis remained active. There was occasional upper abdominal pain, without cramps. Ascites appeared. There was no icterus. A right femoral phlebotrombosis developed. The patient remained weak and despondent. He became nauseated and vomited.

all food. The temperature remained normal. He went into coma and expired on the twentieth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. JOSEPH AUB: This patient had a prolonged disease. It could have been ulcerative colitis or tuberculosis or possibly amebic infection. The unequivocal statement is made that this man had an infection with the Flexner organism. A Flexner infection would not have lasted so long, but it may well have been an ulcerative colitis following a Flexner infection.

The description of the tongue indicates a vitamin deficiency, which is to be expected in this disease.

"A superficial, lobulated, firm, nontender mass was felt in the right upper quadrant." I take that to be the liver. We know that the liver was enlarged three years previously. Of course, it may have been a neoplasm in the liver, but I assume that the mass represented a large liver.

This man undoubtedly had an ulcerative colitis, which may or may not have started from the Flexner infection thirteen years before. A lot of work has been done on this causal relation, although few cases have been proved to follow this infection, and the organism does not appear to be present in many cases of established colitis. At any rate, this man had had ulcerative colitis since he was twelve years old. We must then go into the refinements of the case, where we are apt to be wrong. Everything that Dr. Chapman said in discussing his case holds for this one, and I am not going to repeat. This is not a case of regional ileitis, because the whole large bowel was involved. The crux of the problem is, What did this patient die of, in addition to the ulcerative colitis, and why did he have a large liver for three years?

Are any x-ray films available?

DR. CASTLEMAN: None were taken on the final admission, and the previous ones are not available.

DR. AUB: When the cecum and ascending colon are so markedly involved, one always thinks of tuberculosis of the large bowel. This lesion started in a twelve-year-old child and might well have been due to tuberculosis. With chronic ulcerative colitis, many polyps form in the cicatricial tissue, and in these areas neoplasm develops at least four times as frequently as it does normally. Ulcerative colitis is certainly one of the precancerous lesions, and the presence of cancer should always be considered in protracted cases. This young man might have had a cancer, but he had a large liver for three years before he died, and I think that it is highly unlikely that a neoplasm from a polyp, even though it may be dormant for a long time, could have reached the stage of metastasizing to the liver and could have remained there for three years before his death. I am willing to rule that out, saying that, although he may have had a carcinoma, the

large liver, which is the crux of this problem, was not due to a neoplasm. The clubbing of the fingers might have been caused by the chronic ulcerative colitis and vitamin deficiency or might have been due to liver damage, although I think that the former is the more probable.

Let us discuss the large liver further. Was this cirrhosis? It might have been a cirrhosis dependent on chronic vitamin B deficiency, the type of cirrhosis that can be produced in the laboratory by an inadequate diet plus a toxin of some sort. It could have been that, but at the end of three years, if it was the usual type of portal cirrhosis, the liver should not have been so large. The diagnosis is a difficult choice between cirrhosis of the liver and amyloid disease associated with chronic infection, such as tuberculosis of the large bowel. Amyloid disease can produce this picture, in fact, the amyloid disease sometimes includes the large bowel. The difficulty is that no albumin was found in the urine, which is against the diagnosis of amyloid disease, but there are cases of amyloid disease that do not involve the kidney, which therefore do not have albumin in the urine.

I think that the liver was seriously damaged but not so severely that there developed a high amino acid concentration in the blood stream. At least the nonprotein nitrogen was normal. That he had something wrong with the blood flow through the liver is suggested by the hemorrhoids, the phlebitis and the ascites.

I am perfectly willing to make a diagnosis of chronic ulcerative colitis. This was probably on the basis of the Flexner infection, but it may well have been of tuberculous origin. The large liver was either cirrhotic or amyloid, and I shall say that it was amyloid, although I am probably wrong because it is relatively rare. The amyloid disease did not involve the kidney, although it may have involved the bowel. I think that he also had thrombophlebitis, which was probably ascending and may well have involved the lower veins in the abdomen. Since he kept on urinating, it is probable that it had not reached the kidney veins. He had ascites and vitamin deficiency.

DR. EARLE M. CHAPMAN: I should like to know why Dr. Aub did not consider pylephlebitis, since the man had chronic infection in the bowel, thrombophlebitis and a "sick" liver. He may have had an infection in the portal system.

DR. AUB: He may have had.

DR. JACOB LERMAN: The patient had no fever.

DR. AUB: The terminal ascites is interesting. I did not mention several things. Of course, one can always go far afield and bring in everything just to be sure of mentioning what might turn out to be the right diagnosis. These patients are apt to have local perforation of the intestine. But this one continued to have intestinal peristalsis until he died, so it is unlikely that he had a perforation.

I doubt that the ascites was due to pylephlebitis, but I do not know

DR LERMAN I should like to consider hepatoma on the basis of an old cirrhosis

CLINICAL DIAGNOSES

Chronic ulcerative colitis
Carcinoma of colon

DR AUB'S DIAGNOSES

Chronic ulcerative colitis
Tuberculosis of large bowel, with amyloid disease of liver?
Thrombophlebitis
Vitamin deficiency
Ascites

ANATOMICAL DIAGNOSES

Chronic ulcerative colitis and ileitis.
Adenocarcinoma of colon (splenic flexure and ileocecal region), with metastases to regional lymph nodes and liver
Acute bacterial endocarditis mitral valve
Septic infarcts of heart, kidneys and spleen

PATHOLOGICAL DISCUSSION

DR CASTLEMAN The autopsy on this man showed an extremely severe chronic ulcerative colitis. There were also numerous ulcerations in the last 30 cm of ileum. The large bowel was thickened, and many of the ulcers were partially or completely healed. The rugal folds were thick. In the region of the ileocecal valve was an annular lesion about 6 cm in length and about 1 cm in thickness, which on section was grayish white. It had extended through the serosa and had become adherent to several enlarged nodes, which were also grayish white and obviously neoplastic. A similar lesion was found in the region of the splenic flexure. This seemed to be more invasive than the one in the region of the cecum. Sections showed the ileocecal lesion microscopically to be a low-grade adenocarcinoma, whereas the one in the splenic flexure was an extremely malignant tumor, showing no acinar arrangement and invasion of the veins throughout that portion of the bowel. The liver was tremendous in size, weighing 4200 gm, and was filled with metastases. There was no cirrhosis.

It is interesting that before this patient died a peritoneoscopy was performed, and we made a diagnosis of hepatoma on a biopsy of one of these nodules. The reason for this erroneous diagnosis, in retrospect, is that the tumor cells were tremendous in size, some of them having four or five nuclei and having a definite eosinophilic cytoplasm, such as one sees in hepatoma. Also, even in this small biopsy specimen, we found invasion of the hepatic veins, which is quite the rule in hepatoma. When

we compared sections of the biopsy with those of the tumor in the region of the splenic flexure, it was apparent that the cells were the same.

On the mitral valve were a large number of bacterial thrombi from which emboli had gone to both kidneys, the spleen and also the coronary arteries. There was a large focus of septic infarction in the heart, and many smaller ones in the kidneys and spleen.

So here we have another case of chronic ulcerative colitis in which two carcinomas developed. You probably know that Barger of the Mayo Clinic has been writing for years about the association of ulcerative colitis and carcinoma. His series is, I believe, the largest. In one reported in 1928, he claimed that 10 per cent of the cases of ulcerative colitis have true adenomatous polyps and that 2 per cent develop carcinoma, the carcinoma apparently developing through the stage of adenomatous polyps, in other words, there is first a pseudopolyp, just a tab of mucosa surrounding an area of ulceration, then the pseudopolyp develops into a true adenomatous polyp, and finally the adenomatous polyp becomes malignant. Barger² has recently reported 30 more cases. It is interesting that the average length of time from the onset of the ulcerative colitis to the appearance of the carcinoma is seventeen years. In the cases that we have discussed here today the time interval in one is eleven and in the other fifteen years. I believe that in the last ten years we have had 3 or 4 other cases of carcinoma developing on ulcerative colitis. As Dr Aub stated, this certainly is a definite hazard in a patient with long-standing ulcerative colitis, especially if he has exacerbations of the colitis, since healing and regeneration of the epithelium may lead to the development of a carcinoma.

DR AUB You have not explained the big liver that had been noted three years previously.

DR CASTLEMAN Most of our cases with ulcerative colitis that come to autopsy have tremendous fatty livers.

The x-ray appearance two or three years before entry was probably due to a low-grade adenocarcinoma in the ileocecal valve. He may have had that for a couple of years, but certainly the one in the region of the splenic flexure was a recent development. It is one of the most rapidly growing carcinomas of the bowel that I have ever seen.

DR LERMAN You are definite that it was not a hepatoma?

DR CASTLEMAN Yes.

DR AUB There was no cirrhosis and no evidence of amyloid disease?

DR CASTLEMAN No.

DR CHAPMAN I think it is instructive that Dr Aub and I both missed the diagnosis. I am sorry that Dr McKittrick is not here, because I should like to know the clinical implications that he would

stress at this point in regard to the way we should take care of these patients with chronic ulcerative colitis. Too often they have an ileostomy and are allowed to go on with the ileostomy, because they are much better, we allow the bowel to lie dormant, which is perhaps not the right thing to do. Perhaps a colectomy should be performed, as Dr McKittrick has done so often. The colon in ulcerative colitis is frequently the site of cancer. That is the one clinical lesson we ought to carry away with us.

DR. CASTLEMAN: I believe that the practice in the hospital now is that if, after ileostomy, a patient continues to have attacks, colectomy is indicated then and not fifteen or seventeen years later, when it may be too late.

ADDENDUM

DR. LELAND S. MCKITTRICK: The problem of carcinoma of the bowel arising in cases of long-standing chronic ulcerative colitis is an important and disturbing one. My own experience with cancer in these patients is not a large one. I have probably seen 5 or 6 such cases, but in only 1 of these was the carcinoma operable. I do not know the operability in the group that Bargen has described but I suspect that it was low. This is particularly true after an ileostomy has been performed, because the symptoms of obstruction, which are frequently so im-

portant in the diagnosis of cancer of the large bowel, are absent and because the bleeding that these patients often have may be misinterpreted as being due to the colitis. Dr. Chester M. Jones and I have frequently discussed the possibility of annual or semiannual examination of the bowel by a barium enema, but this is not wholly practical, one reason being that not infrequently after ileostomy the bowel does not quite empty itself and the barium remains inspissated for indefinite periods.

I feel strongly that the indications for colectomy should be broadened. The mortality following colectomy done as an elective procedure is low. Certainly the demonstration of persistent polyps or pseudopolyps is, I believe, a definite indication for colectomy. At the present time it is my opinion that any large bowel which, after ileostomy, shows persistent evidence of activity of the disease should probably be removed. In many of these cases, the rectum and lower sigmoid are left in place, thus allowing an opportunity for reestablishment of continuity at a later time, should some method of curing the disease be developed.

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2. Bargen J. A. Chronic ulcerative colitis associated with malignant disease. *Arch Surg* 17: 61-66, 1928.

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REFRESHER COURSES

ALTHOUGH the three medical schools and most of the teaching hospitals in Greater Boston, as well as other hospitals in Massachusetts, have signified their willingness to participate in a program designed to provide refresher courses for discharged medical officers and stale civilian physicians, the consummation of the scheme within a period short of many months appears to be impossible. The obstacle is a lack of teaching personnel, and until such a time as the Army and Navy release an appreciable number of medical officers capable of effective teaching, this well conceived and extremely necessary program must be postponed.

With the end of combat, the need for medical officers must have dropped appreciably, and there

seems to be no valid reason for not revising the tables of organization of both the Army and Navy so that they are on a peacetime basis. It is obvious that a certain number of medical officers are needed for the care of the armed forces in occupied areas and of those at permanent Army installations and on the ships of the Navy. On the other hand, these men represent only a small percentage of those who have been serving with the Army and Navy. It will undoubtedly take time to return many of these men to the United States, and more time will be consumed by the formalities of release or discharge, but the sooner this is accomplished the sooner medicine, including postgraduate instruction, will return to a reasonably normal basis.

For the time being, refresher courses must, as a rule, be limited to short periods of intensive teaching, such as the courses to be given this fall in various communities in the Worcester and Springfield areas by teams of instructors under the sponsorship of the Subcommittee on Medical Education, Committee on Postwar Planning. Other examples are the three-day course given periodically at the New England Deaconess Hospital, which covers all the various aspects of diabetes mellitus, and the course in medicine for general practitioners that is to be given by members of the Lahey Clinic in November. This type of instruction is not suitable for the physician who desires extensive postgraduate instruction or training in some particular aspect of medicine, but at the moment, it is about all that can be expected.

ENGLAND WANTS MORE AND BETTER MILK

THE Mother of Parliaments, according to a leading article in the April 21 issue of the *Lancet*, is taking seriously the dairy situation in England—the shortage of milk, the shortage of cows, the shortage of veterinarians and the high incidence of diseased cattle. At present the daily per capita milk consumption in Great Britain is 0.58 pint. Before the war it was 0.45 pint, and a suggested target at which to aim has been set at 0.75 pint or, ideally, a full pint.

The discussion, which took place on April 11, was initiated by Viscount Bledisloe in the House of Lords with the statement, "In the matter of the general milk-supply, its quality, the individual milk consumption, the milk yield per cow, bovine disease, veterinary treatment and the number and qualifications of our veterinarians, Great Britain compares unfavourably with most of the other civilised countries of the world, including indeed some uncivilised countries, such as Germany."

One of the alarming statements was that, although various efforts had increased the milk supply by 12 per cent from 1939 to 1945, the prevalence of mastitis, contagious abortion, sterility and Johne's disease had reduced annual production by about 200,000,000 gallons, in addition to the loss of cattle through foot-and-mouth disease. Among the recommendations proposed were the offering of a bonus to increase the number of tuberculin-tested herds, a survey of the incidence of cattle disease and an increase in the numbers of tuberculin-tested herds to the point where eventually milk from a herd that is not free from tuberculosis would not be accepted for human consumption. A further recommendation was that veterinary study be given full university status and that veterinary research should be established in all training centers.

Particularly startling to Americans are the statement that 40 per cent of the cattle of the United Kingdom are infected with tuberculosis and the apparent distrust in which pasteurization is still held. Thus, it is stated in the section "Parliament" of the same issue of the *Lancet*: "Lord Moran applauded Lord Bledisloe's exquisite tact in not mentioning pasteurization. It had always seemed to him that if milk contained organisms and if those organisms produced disease, then the public, when it understood the position, would demand that those organisms be removed. Our target must therefore be to sell milk free from disease or to pasteurize it. If it was sold and bottled on the farm where there was no disease, then pasteurization would die a natural death."

In this country the eradication of bovine tuberculosis has gone steadily forward to the point where now in Massachusetts, with all cattle tested, the rate of incidence is only 0.2 per cent, the rate being

0.5 per cent or less for the country as a whole*. In addition, pasteurization, far from being allowed to die a natural death, has steadily increased until it is practically a *sine qua non* of clean milk. In fact, on September 30, 1943, the health commissioner of Boston took the final step in requiring all milk sold in this city, even from certified herds, to be pasteurized.

*Tuberculosis Eradication Division, United States Department of Agriculture. Personal communication.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

CANNON — Walter Bradford Cannon, M.D., of Cambridge died at Franklin, New Hampshire, on October 1. He was in his seventy-fourth year.

Dr. Cannon received his degree from Harvard Medical School in 1900 and had served there as George Higginson Professor of Physiology from 1906 to 1942. During World War I he was chairman of the Committee on Physiology of the National Research Council, and went abroad in May 1917, with the Harvard Hospital Unit. He served overseas until January, 1919, and was discharged with the rank of lieutenant-colonel. In June, 1919, the British government conferred on him the Cross of the Companion of the Bath "for meritorious service for the Allied cause." He was also awarded a citation by General Pershing for instruction in shock treatment in the AEF. He was a trustee and member of the Executive Committee of the Harvard Medical School of China and in 1942 was elected chairman of the Massachusetts Branch of the American Bureau of Medical Aid to China.

Dr. Cannon was a member of the American Medical Association, the American Association for the Advancement of Science, the American Physiological Society, the Society for Experimental Biology and Medicine, the American Gastroenterological Association, the American Philosophical Society of Philadelphia, the American Psychological Association and the Boston Society of Medical Sciences.

His widow, four daughters and a son survive.

HEARN — Walter L. Hearn, M.D., of Lynn, died September 30. He was in his sixty-eighth year.

Dr. Hearn received his degree from Harvard Medical School in 1902. During his career he served on the staffs of the Boston Lying-in Hospital, the Children's Hospital, the Massachusetts General Hospital and Lynn Hospital. He was chief surgeon of the Lynn Cancer Clinic, and in recent years had been Lynn school physician.

MEDICOLEGAL ABSTRACT

Right to Compensation. Right of a physician consulted at the request of a company to charge the patient. The physician sued the patient and her husband for the reasonable value of his professional services, and the defendants prevailed even though they admitted that the services were performed and that the amount claimed was their reasonable value.

The patient sustained a fall in a retail store, and the store manager directed her to see the plaintiff and have him perform such professional services as were necessary due to the fall or accident. The

patient and her husband consulted the physician only after the store manager advised her that she would be put to no expense but that such professional treatment would be "all gratis," and they consulted him only because they had been so directed by the manager. There was evidence that the physician knew of the arrangement before he treated the patient.

It was clear that neither the patient nor her husband had agreed expressly to pay the physician, but the court thought he could recover the reasonable value of his services from the patient if there was any implied contract to pay for them, and under the statute in force there would be such a contract if its existence and terms were "manifested by conduct." The court held that no such contract was implied when the physician assented to the arrangement that had been made with the store. The court said:

When plaintiff proceeded to treat Mrs. Iverson knowing of the agreement between her and Woolworth's and at Woolworth's request, such conduct rather than implying an understanding between physician and patient that the patient will pay the reasonable value of the services performed, implies, in our opinion, an agreement by the physician to perform the services according to the conditions and terms under which he is consulted and asked to perform the service.

The court made it clear that it was not holding that the physician was necessarily precluded from charging the patient for his services if he had rendered the services at the request of the store. The point was only that the physician could not charge the patient if he had performed the services under an arrangement that the patient should not have to pay for them. — (*Ophelm v Iverson*, So. Dakota, 16 N. W. [2d] 440 [1944].)

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THE ABSORPTION, EXCRETION AND TOXICITY OF STREPTOMYCIN IN MAN*

DONALD G. ANDERSON, M.D.,† and MARJORIE JEWELL, A.B.‡

BOSTON

IN JANUARY, 1944, Schatz, Bugie and Waxman¹ described the isolation of a new antibacterial substance from the culture filtrate of *Actinomyces griseus*. They named this substance "streptomycin" and reported that it had a marked antibacterial action in vitro against many gram-negative and gram-positive bacteria. According to its discoverers, streptomycin resembled streptomycin, another antibacterial agent isolated in 1942,² but had a wider bacteriostatic spectrum and was quantitatively more active against certain organisms and less toxic for animals.

Several studies³⁻⁹ have now been reported in which it has been shown that streptomycin is sufficiently effective in vivo in the treatment of experimental infections in animals with various gram-negative bacteria and *Mycobacterium tuberculosis* to warrant an extended clinical investigation of its value in the treatment of human infections. To date, only one report¹⁰ has been published describing the use of streptomycin in the treatment of established infections in man. Other clinical studies are now being carried out by various investigators, and as the production of streptomycin increases, further information regarding its effectiveness as a chemotherapeutic agent should soon be forthcoming.

The purpose of this paper is to report certain preliminary studies carried out on the absorption and excretion of streptomycin in man. In addition, brief mention is made of 3 cases in which the drug was used therapeutically. Finally, the toxic reactions observed are described.

MATERIALS AND METHODS

All subjects used for the pharmacologic studies were adult ward patients who presented no evidence of any impairment of renal function.

*From the Evans Memorial Massachusetts Memorial Hospitals and the Department of Medicine, Boston University School of Medicine. The streptomycin used in this study was supplied through the courtesy of Merck and Company, Rahway, New Jersey, from supplies allocated to the Committee on Chemotherapeutics and Other Agents, National Research Council for investigations on the toxicology, absorption and excretion of streptomycin.

†Instructor in medicine, Boston University School of Medicine; research fellow in medicine, Evans Memorial Massachusetts Memorial Hospitals.

‡Laboratory assistant, Evans Memorial Massachusetts Memorial Hospitals.

Streptomycin was dissolved in distilled water for intravenous, intramuscular and subcutaneous administration in concentrations varying from 50,000 to 150,000 units per cubic centimeter. The solutions used for intrathecal administration varied in concentration from 2500 to 5000 units per cubic centimeter. Although streptomycin has been shown to be relatively heat stable and to be capable of withstanding room temperatures for extended periods of time, the various solutions of the drug were stored at 5°C until time of use.

The samples of blood that were assayed for streptomycin were taken under sterile precautions and allowed to clot in sterile tubes. The serum was then separated by centrifugalization.

All studies on the urinary excretion of streptomycin were carried out in male patients, the patients voiding into sterile containers.

All samples of body fluids were stored at 5°C until they were tested. All but a few specimens were tested on the same day that they were obtained.

The method of assay used was the cup-plate method described by Stebbins and Robinson,¹¹ in which *Staphylococcus aureus* (Strain SM) is employed as the test organism. The only modification of the method was the use of horse serum instead of the patient's serum to dilute the standard solutions used in assaying serum specimens. This modification was made for the sake of convenience after it had been determined that the substitution of horse serum did not alter the diameter of the zone of inhibition obtained with the standard amounts of the drug used in the method.

This method has proved to be extremely satisfactory for the determination of concentrations of streptomycin in body fluids varying from 1 to 12 units per cubic centimeter, and only slightly less satisfactory for concentrations up to 20 units per cubic centimeter. Within these ranges relatively consistent and reproducible results have been obtained. When higher or lower concentrations of streptomycin have been encountered, the results of replicate tests have shown less consistency. The determinations done on urine specimens, in which

patient and her husband consulted the physician only after the store manager advised her that she would be put to no expense but that such professional treatment would be "all gratis," and they consulted him only because they had been so directed by the manager. There was evidence that the physician knew of the arrangement before he treated the patient.

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of 1 unit per cubic centimeter was still detectable in the serum at the end of eight hours. After the was to produce somewhat higher serum levels than those observed at similar intervals after a single in-

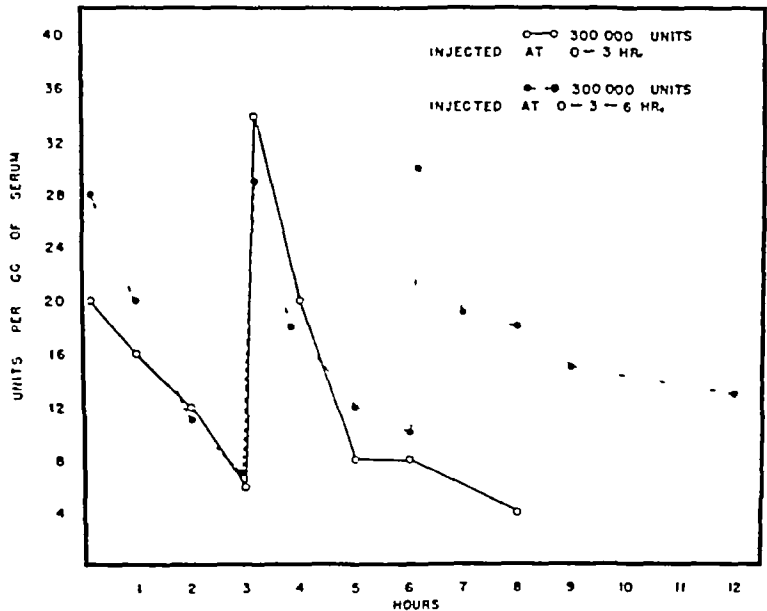


FIGURE 2 Concentrations of Streptomycin in Serum following Multiple Intravenous Injections at Three-Hour Intervals

injection of 600,000 units, the largest dose administered, the serum still contained 3 units per cubic centimeter at the end of eleven hours

jection. The higher levels so obtained appeared merely to reflect the accumulation of the drug in the body.

Intramuscular Administration

Figure 2 shows the serum concentrations in 2 patients receiving multiple intravenous injections

Figure 3 shows the concentrations of the drug

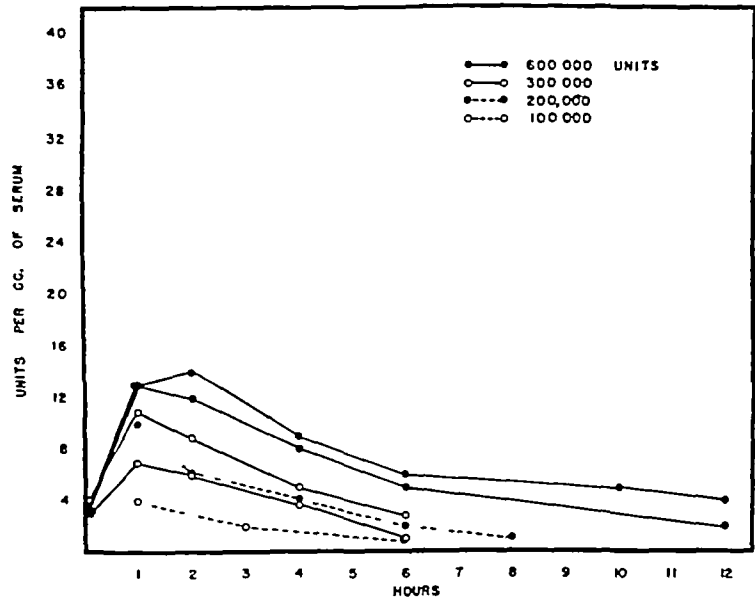


FIGURE 3 Concentrations of Streptomycin in Serum following Intramuscular Injection of Varying Doses

of 300,000 units each at three-hour intervals. The effect of repeating the injections at short intervals

observed in the serum at varying intervals after the intramuscular administration of single injections into

high concentrations of streptomycin were frequently encountered, probably have a fairly high margin of error and should be considered as representing only approximate values. The only other significant problem met within the cup-plate method was that of occasional technical difficulty in securing even, regular zones of inhibition about the cups.

In the pharmacologic studies, all determinations were made in duplicate and many of them in triplicate. When irregularity of the zones of inhibition rendered a test unsatisfactory, it was repeated. The final value assigned to any determination was the average of the replicates computed to the nearest whole unit.

The streptomycin unit has been defined by Robinson² and his associates⁴ as that quantity of the anti-

antibacterial activity for this test organism as does a unit of streptomycin.

ABSORPTION OF STREPTOMYCIN WITH VARIOUS ROUTES OF ADMINISTRATION

Oral Administration

Six hundred thousand units of streptomycin dissolved in 100 cc of tap water was administered orally to 1 patient in the fasting state. The serum was tested for its streptomycin content at frequent intervals during the next twelve hours. *No drug was detected in the serum at any time.* A solution containing 20 units of streptomycin per cubic centimeter was then incubated at 37°C for three hours with an equal volume of gastric juice containing free

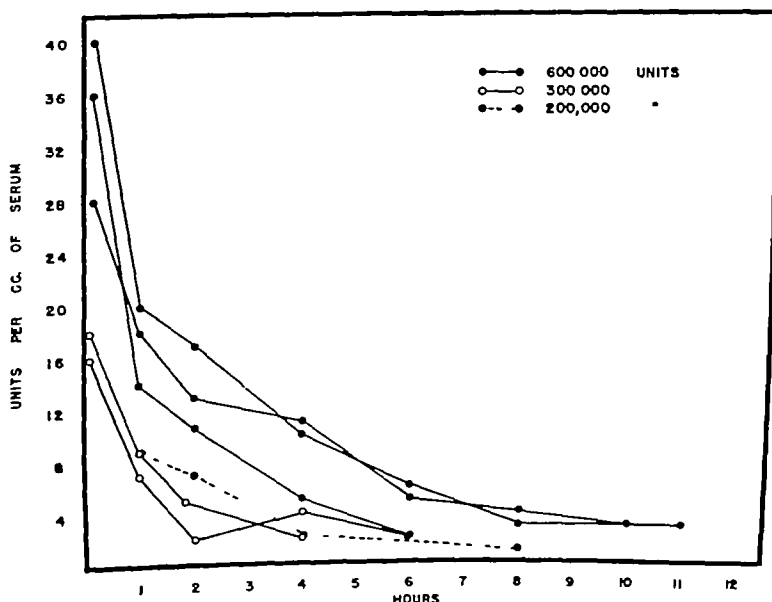


FIGURE 1 Concentrations of Streptomycin in Serum following the Intravenous Injection of Varying Doses

biotic agent that inhibits the growth of a given strain of *Escherichia coli* in 1 cc of nutrient broth or agar. They have reported the production of preparations of streptomycin that contain 500 units per milligram.

For the purposes of orientation, it should be pointed out that a unit of streptomycin represents a much smaller amount of antibacterial activity than does a unit of penicillin. Thus, when the action of the two substances is studied against *Staph aureus* (Strain SM), an organism against which both drugs are active, it is found that the growth of this organism is just completely inhibited by 0.08 units of penicillin, whereas the smallest amount of streptomycin that causes complete inhibition is 1 unit. It is therefore apparent that a unit of penicillin represents approximately twelve times as much

hydrochloric acid. Assay of the mixture at the end of the period of incubation showed that the exposure to gastric juice for three hours had resulted in no loss of the drug's activity.

Intravenous Administration

Figure 1 shows the concentrations of streptomycin in the serum at varying intervals after the intravenous injection of single doses of the drug in different cases. The highest levels were obtained within five minutes after injection. Individual variations were observed, but the levels were in general proportional to the amount injected. During the first hour after injection the concentration in the serum decreased rapidly, but in the succeeding hours the fall was more gradual. With the smallest dose administered, 200,000 units, a concentration

increased to 200,000 units every 3 hours. This dosage was continued for the next 7 days, at which time treatment was discontinued.

From the chart it can be seen that the blood culture became permanently negative before the dosage was increased from 12,000 to 200,000 units every 3 hours. The urine culture

until 6 days after streptomycin was discontinued. From then on the patient appeared to have recovered fully from the acute illness, and her subsequent convalescence was uneventful.

Comment: The evaluation of the effect of the streptomycin therapy in this case is difficult. The patient's clinical

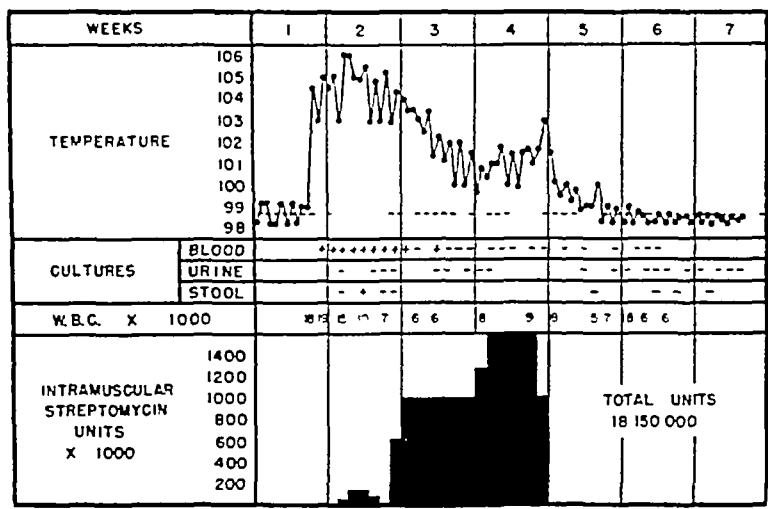


FIGURE 4 Chart of a Patient with Typhoid Fever (Case 1) Treated with Streptomycin

The patient's clinical and bacteriologic course was suggestive, but not conclusive, of a definite therapeutic response to streptomycin

was never positive, and except for one positive culture on the 6th day of the illness, *E. typhosus* was never recovered from the stool.

The temperature, which had been sustained between 103 and 104°F during the first 9 days of the illness, declined by 1°F during the 1st week of treatment with the larger doses

and bacteriologic course is suggestive but not conclusive, of a definite therapeutic response to streptomycin.

This patient received a total of 18,150,000 units of streptomycin over a period of 20 days. During this time repeated blood counts and urinalyses showed no evidence that streptomycin had any harmful effect on the hematopoietic system

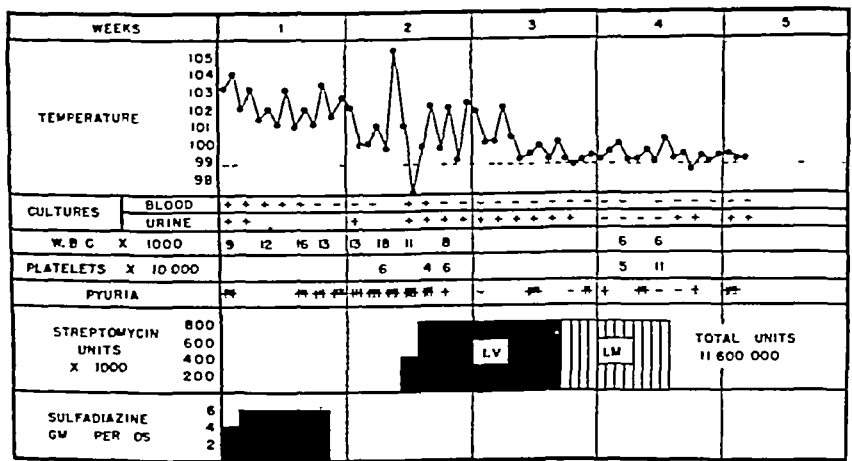


FIGURE 5 Chart of a Patient with Prolonged Bacteremia Caused by a Group B Salmonella (Case 2) Treated with Streptomycin

The illness was complicated by thrombocytopenia with severe epistaxes. The effect of streptomycin therapy was difficult to evaluate

During the 2nd week it gradually rose again to 103°F but fell to normal the day after streptomycin was discontinued. Thereafter it remained below 100°F.

Symptomatically the response to treatment was not striking. The patient remained lethargic and suffered from severe anorexia until she had received 1,000,000 units of streptomycin daily for 7 days. At that time, the 15th day of the illness, she began to have a desire for food and appeared somewhat more alert. Thereafter there was slow but progressive improvement. Her marked lethargy persisted, however,

or on the kidneys. The patient did complain continually of pain following the intramuscular injections, and during the last 2 weeks of treatment the buttocks were indurated and extremely tender. In view of the prompt return of the temperature to normal after streptomycin was discontinued, it seems reasonable to ascribe the rising fever during the last week of treatment to the drug.

CASE 2 (Fig 5) J. G., a 46-year-old American Indian, had had diabetes mellitus for 7 years. Fifteen days before ad-

the gluteal muscles. The only essential difference between these results and those observed after intravenous injection was that the concentrations found in the serum five minutes after intramuscular injection were much lower. The height of the levels at the other points on the curve and the persistence of the drug in the serum after a given dose did not vary significantly with the route of administration.

EXCRETION OF STREPTOMYCIN IN THE URINE

In Table 1 is shown the total twenty-four-hour excretion of streptomycin in the urine as observed in 4 subjects. The amount of drug excreted in

TABLE 1 *Twenty-Four-Hour Excretion of Single Doses of Streptomycin in the Urine*

Dose	ROUTE OF INJECTION	URINARY EXCRETION
units		%
600 000	Intravenous	50
600 000	Intravenous	66
600 000	Intravenous	46
600 000	Intramuscular	64
Average		57

twenty-four hours varied from 46 to 66 per cent and averaged 57 per cent of the dose injected.

The rate of excretion at various intervals after injection is shown in Table 2. Although excretion was

TABLE 2 *Excretion of a Single Dose of Streptomycin in the Urine at Varying Intervals after Administration*

Dose	ROUTE OF INJECTION	0-1	URINARY EXCRETION IN HOURS				TOTAL EXCRETION
units		%	2-3	4-11	12-23	24-30	%
200 000	Intramuscular	33	30	Not done	Not done	Not done	63 (4 hr)
300 000	Intramuscular	33	15	20	3	1	72 (30 hr)
600 000	Intramuscular	39	16	32	Not done	Not done	87 (12 hr)

greatest during the first four hours after administration, one fifth to one third of the dose injected was not excreted until between the fourth and the twelfth hour. The excretion during the interval between the twelfth and the twenty-fourth hour was studied in only 1 case, in which only very small amounts of streptomycin appeared in the urine after the twelfth hour. Traces of the drug, however, could still be detected between the twenty-fourth and the thirtieth hour after injection.

From these figures it can be concluded that the urinary excretion of streptomycin is significantly slower than that of penicillin, since after intramuscular or intravenous injection an average of 60 per cent of the dose of penicillin injected can be recovered in the urine within one hour. Likewise, the excretion of a single dose of penicillin is nearly complete by the end of four hours.

DIFFUSION OF STREPTOMYCIN INTO SPINAL FLUID

Studies of the diffusion of streptomycin from the blood into the spinal fluid were carried out in a patient suspected of having tuberculous meningitis. The cerebrospinal fluid was tested for its streptomycin content on four separate days at intervals varying from two to eight and a half hours after the

parenteral administration of doses of 200,000 and 300,000 units of streptomycin. Simultaneous serum levels were determined, and by coincidence were 5 units per cubic centimeter on each occasion. On

TABLE 3 *Streptomycin Levels in the Cerebrospinal Fluid after Intrathecal Administration**

Dose	24-Hr. SPINAL FLUID LEVEL	24-Hr. SERUM LEVEL
units	units/cc	units/cc
5 000	6	1
10 000	7	2
10 000	5	4
15 000	6	4
15 000	7	2
20 000	14	2

*Intramuscular therapy at a dosage of 300 000 units every 12 hours was being administered simultaneously.

two days the spinal fluid showed merely a trace of streptomycin, whereas on the other two days readings of 1 unit per cubic centimeter were obtained.

Streptomycin was then administered intrathecally to the same patient. Intramuscular therapy at a dosage of 300,000 units every twelve hours was administered simultaneously. The levels obtained in the cerebrospinal fluid twenty-four hours after the administration of various doses and the simultaneous serum levels are shown in Table 3. These results indicate that following the intrathecal ad-

ministration of streptomycin, the absorption of the drug from the subarachnoid space is not complete by the end of twenty-four hours.

CASE REPORTS

To date we have had an opportunity to administer streptomycin in therapeutic doses to only 3 patients. These cases are reported briefly, chiefly to illustrate the apparent lack of significant toxicity following the prolonged administration of streptomycin.

CASE 1 (Fig. 4). V. H., a 17-year-old Negroess, entered the hospital for fusion of the right knee because of tuberculous synovitis. For the first 2 weeks after operation, convalescence was satisfactory. On the 15th postoperative day, there was a sudden chill and the temperature rose to 104.4°F. There were no localizing signs or symptoms. A blood culture was obtained the following day and 48 hours later was reported to be positive for *Eberthella typhosus*. Subsequent studies showed that this organism was completely inhibited in vitro by 12 units of streptomycin per cubic centimeter of media.

When the positive blood culture was reported, streptomycin therapy was started at a dosage of 30 (0) units intramuscularly every 4 hours. After 72 hours the supply of streptomycin was temporarily exhausted. Twenty-four hours later, the 9th day of the illness, a fresh supply of drug was received and treatment was resumed at a dosage of 125,000 units intramuscularly every 3 hours. After this dosage had been administered for 48 hours the blood culture became negative. A blood culture taken 2 days later, however, proved to be positive. When this report was received the dosage was

centimeter produced pain, tenderness and moderate swelling of the tissues at the site of the injection. The pain lasted for more than an hour and some tenderness and swelling persisted for forty-eight hours.

The intrathecal administration of streptomycin solutions containing 5000 units per cubic centimeter in amounts up to 4 cc produced no signs of meningeal irritation. After repeated intrathecal injections over a period of several weeks 1 patient complained of pain in the back radiating down the posterior aspect of both thighs on coughing or moving.

SUMMARY AND CONCLUSIONS

From this study the following conclusions have been drawn:

Streptomycin is not absorbed after oral administration in amounts sufficient to produce detectable concentrations of the drug in the serum.

The failure of the drug to be absorbed from the gastrointestinal tract is not due to the inactivation of streptomycin by the gastric juice.

The curves of the serum concentrations of the drug after the intramuscular or intravenous injection of a given amount of streptomycin do not differ significantly except during the first few minutes after injection.

Following the intramuscular or intravenous administration of a single dose of streptomycin 46 to 87 per cent of the dose injected can be recovered in the urine within twenty-four hours.

Streptomycin is excreted more slowly by the kidneys than is penicillin. It appears likely that effective blood levels of streptomycin can be maintained by administering the drug at intervals of six to eight hours.

In patients with meningitis, streptomycin diffuses to a slight extent from the blood into the cerebrospinal fluid.

The intrathecal administration of streptomycin in doses up to 20,000 units does not produce signs of meningeal irritation. With doses of 10,000 to 20,000 units, an appreciable concentration of the drug can be maintained in the cerebrospinal fluid for at least twenty-four hours.

No serious toxic reactions apparently follow the injection of single doses of streptomycin in amounts up to 600,000 units or after the continued administration of the drug for periods of two to three weeks in doses totaling 2,725,000 to 18,150,000 units.

The intravenous and subcutaneous injection of concentrated solutions of the present preparations of streptomycin causes too much discomfort to warrant the use of these methods of administration.

The drug can be administered in an intravenous infusion without the production of unpleasant symptoms.

Intramuscular injections are fairly well tolerated for periods up to one to two weeks. Therapy continued beyond these times may cause severe discomfort.

Three cases of infection due to a gram-negative bacillus and treated with streptomycin are reported, no conclusions concerning the efficacy of streptomycin can be drawn from them.

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mission to the hospital he had had a shaking chill and had developed dull aching pain in both loins. The next day the urine became cloudy and there was burning pain on urination. The fever, pain and dysuria persisted for the next 2 weeks, during which time the patient remained in bed at home without receiving specific therapy. At the end of that time he was referred to the hospital by his physician.

On physical examination the patient appeared acutely ill. The only positive physical findings of significance were marked bilateral costovertebral-angle tenderness and marked prostatic tenderness on rectal examination. In addition, the prostate gland was moderately enlarged and boggy. There were no signs of a prostatic abscess.

Blood and urine cultures on entry to the hospital were both positive for a gram-negative bacillus that gave the fermentation reactions of a Group B *Salmonella*. (Further studies to complete its identification are being carried out.) The organism was found to be completely inhibited in vitro by 4 units of streptomycin per cubic centimeter of medium.

Immediately on admission the patient was given sulfadiazine, 1 gm every 4 hours. On the 6th day of treatment, the blood culture became negative and remained negative for the next 4 days. Symptomatically the patient was markedly improved, the costovertebral-angle pain and the dysuria having entirely disappeared. Improvement continued until the 8th hospital day, when there began a series of severe spontaneous epistaxes. Within 48 hours the hematocrit fell from 40 to 30 per cent. The platelets were markedly reduced, numbering only 64,000 per cubic millimeter. During the next 36 hours the patient received 1500 cc of whole blood by transfusion, with only a slight decrease in the amount of bleeding.

Treatment with streptomycin was started on the 11th hospital day at a dosage of 200,000 units intravenously every 6 hours. After 9 days of treatment, intravenous therapy was discontinued and the same dosage was given by intramuscular injection. Treatment was continued for another 6 days.

A blood culture taken just before streptomycin was begun and another taken 24 hours later were positive for the same organism that had been recovered from the blood and urine on entry. From that time on, however, all blood cultures were negative. The urine culture remained positive until the last 4 days of treatment and again became positive the day after streptomycin was discontinued.

The temperature remained elevated until the 8th day of treatment. Thereafter it was below 100°F rectally until the last day of treatment, when it rose to 100.4°F for 12 hours. The patient had recovered from his acute discomfort before streptomycin was started, and reliance in judging his progress had to be placed on objective findings.

The epistaxes continued for the first 5 days of streptomycin therapy. On the 3rd day of treatment, numerous petechiae appeared in the skin and conjunctivas and several flame-shaped hemorrhages were seen in the ocular fundi. New petechiae kept appearing for the next 2 days. Thereafter, no new hemorrhagic phenomena were observed. Although no significant rise in the platelet count was observed until the last day of therapy, 50 per cent clot retraction within 2 hours was observed from the 12th day on. Previous to this time the 2-hour clot retraction had never exceeded 20 per cent.

Comment. The evaluation of the effectiveness of streptomycin therapy in this case is even more difficult than that in Case 1. It is entirely possible that the patient would have improved spontaneously without specific therapy. The reappearance of positive urine cultures after the completion of treatment is clear evidence that the drug had not eliminated the infecting organism from the tissues, although it may have played a role in clearing the organism from the blood stream.

This patient received a total of 11,600,000 units of streptomycin over a period of 15 days. As in the first case, no toxic effects on the kidneys or hematopoietic system were observed. A low-grade fever appeared on the last day of treatment and disappeared when streptomycin was withdrawn.

The intravenous injections were at first well tolerated but later caused flushing of the face, intense headache and nausea. The only ill effects from the intramuscular injections were pain and tenderness at the sites of injection.

CASE 3 * The patient was a 5-year-old girl who had meningitis and bacteremia caused by an organism that had all the cultural characteristics of *Haemophilus influenzae* but that could not be typed with either Type A or Type B antiserum. The organism was completely inhibited in vitro by 0.75 units of streptomycin per cubic centimeter of medium.

After 8 weeks of treatment with sulfadiazine and sulfamerazine, the patient was still acutely ill and cultures of the blood and spinal fluid were both positive. Streptomycin therapy was then instituted, the patient receiving a total of 2,725,000 units intramuscularly and 255,000 units intrathecally over a period of 3½ weeks. There was a prompt clinical and bacteriologic response to the administration of the drug and the patient completely recovered.

TOXIC REACTIONS

Repeated examination of the blood in the patients receiving single doses of streptomycin and in those receiving the drug in therapeutic doses failed to reveal any damage to the hematopoietic system. Daily urinalyses, frequent determinations of the blood non-protein nitrogen and the measurement of the daily urine volume likewise indicated that streptomycin in the doses used had no deleterious effect on the kidneys. Although it was not tested for specifically, clinically none of the patients showed any evidence of liver damage.

The administration of single doses of the drug caused no febrile reactions. In Cases 1 and 2, attention has already been called to the fact that the patients had fever, which promptly disappeared when treatment was stopped. No skin eruptions were observed in any patients receiving streptomycin.

When intravenous injections of solutions of streptomycin containing 50,000 to 100,000 units per cubic centimeter were given, the patients almost uniformly complained of a peculiar taste in the mouth and a throbbing headache and showed flushing of the face. A marked flush was usually visible and lasted for two or three minutes after the completion of the injection. The headache usually lasted somewhat longer but disappeared in ten to fifteen minutes. Two patients experienced nausea after the intravenous injection of concentrated solutions. When streptomycin was administered in a slow intravenous infusion, doses up to 500,000 units were given in the course of an hour without producing unpleasant symptoms.

The intramuscular injection of solutions containing 50,000 to 100,000 units per cubic centimeter caused a moderate amount of pain immediately after injection, but the degree of discomfort was not severe. The acute pain usually passed off in fifteen to thirty minutes, but some soreness at the site of the injection persisted for one to several hours after a single injection. When multiple intramuscular injections were given, the buttocks became constantly painful, tender and indurated. These findings persisted for as long as a week after the injections were discontinued. Only rarely did an intramuscular injection produce flushing and headache.

In 1 case, the subcutaneous administration of 2 cc of a solution containing 150,000 units per cubic

*This case is to be reported in detail by Dr. Louis Weinstein in a paper discussing infections caused by atypical strains of *Haemophilus influenzae*.

a better policy to concentrate on the rapid evacuation of the wounded to hospitals in the rear and to postpone the intensive use of the sulfonamide drugs until their arrival there

Now that a more effective and safer chemotherapeutic agent is available for the treatment of infection in the form of penicillin, the question arises whether it can be used in forward operating hospitals. Experiments are being conducted with its local use in wounds, and on their outcome depends the decision whether this method is worth while. As for its general use in the forward hospitals, this appears to be unacceptable except in selected patients who may be held for reasons of safety, because of the difficulty of keeping up the necessary intramuscular or subcutaneous injections during evacuation. On the other hand, penicillin has proved valuable in the treatment of many patients with severely infected wounds after they reach the general hospitals in the rear.

TREATMENT IN REAR HOSPITALS

I have discussed the treatment of the wounded at the front, particularly that of those with compound fractures, because the results of such treatment have a great bearing on the reconstructive surgery that must be done later. The same also applies to the intermediate treatment that is carried on in the general hospitals located in safe areas behind the front, to which the wounded are evacuated following primary treatment. A great contribution to their better care has been made by the improvements in transportation and the wider use of the airplane. These make their evacuation quicker and safer.

The function of these hospitals is to provide medical care of the wounded until they are able to return to active duty or, if it is decided that they cannot be so returned, until they are in sufficiently good condition to make the journey by airplane or ship to the United States. According to a directive of the Surgeon General of the Army, no reconstructive surgical operations are to be performed in foreign theaters of operation and all wounded who require such procedures must be returned to this country. Notwithstanding this limitation on their surgical activities, these hospitals are making important contributions to the treatment of the wounded.

All the patients with injuries involving the bones and joints are the responsibility of the orthopedic surgeons, and they have the task of dealing with infected, malunited and ununited fractures and with the injuries of the joints. So far as invasive infections are concerned, including those from the anaerobic gas-producing organisms or the hemolytic streptococci, these are less frequent and better controlled — by penicillin and the sulfonamide drugs — than was the case in the last war. But the gain in this direction has been counterbalanced by the

increase in severe compound and comminuted fractures of the lower extremities resulting from the extensive use of land mines. Unfortunately, many amputations must still be performed because of vascular injury, extreme structural damage or gas gangrene, but the indications for such mutilating operations are now better known and more quickly recognized than before, so that more lives are saved.

When patients with compound fractures or joint injuries are admitted to these hospitals in the rear, the first step is to remove the plaster casts in which they were transported and to apply traction, either by adhesive strips or when indicated by skeletal pins, in conjunction with suspension splints. Therefore, the surgical objective so far as the fracture is concerned is to secure the best possible alignment of the fragments and to maintain it until either bony union is obtained or the healing progresses sufficiently to permit encasement in plaster without danger of loss of position, thus permitting transportation to the United States.

But the splinting of the fracture is only one part of the management of these battle-incurred compound fractures, the other part is the treatment of the wounds. There has been quite a swing away from the closed plaster or Orr no-dressing technic that was so popular in the early days of the war. Doubtless this has been motivated partly by the development of more efficient methods of chemotherapy, but successful experiments with secondary wound closure have also played a part.

Experience has shown that when a wound is left open with bone fragments exposed in its depths, sooner or later secondary infection develops even when it was clean primarily. The best method of insurance against secondary infection is to seal the wound by a barrier of intact skin and soft tissue. Primary closure cannot be practiced at the field hospitals because of the danger that would be incurred in early evacuation. On the other hand, when the wounds of compound fractures have been thoroughly débrided and the fractures properly splinted, the patients reach the rear hospitals before infection has developed. Under these circumstances secondary closure by suture or by skin grafts may be attempted with little risk, especially when the patient is protected by the administration of sulfadiazine or penicillin. Experience shows that the earlier the closure is attempted the better are the results. The optimum time is from three to five days, but many successful closures have been obtained after longer periods. Preliminary reports indicate that successful results have been accomplished in 75 to 80 per cent of the cases, and that even when the result was a failure little or no harm to the patient resulted.

Some surgeons advocate internal fixation of the fragments by the use of steel bone plates at the time of the closure, but it is too early to evaluate this procedure. The transformation of compound,

RECONSTRUCTIVE SURGERY OF THE WAR WOUNDED*

PHILIP D. WILSON, M.D.†

NEW YORK CITY

THE term "reconstructive surgery" means the making good of physical defects. To reconstruct, according to *Webster's Dictionary*, is "to rebuild, to remodel or to construct again", hence, the term has a mechanical implication that pertains to a large field of orthopedic surgery. It is a term that was born from the last war after experience with the rebuilding of defects to skin, muscle, nerves, bones and joints resulting from war injuries. It thus has a vital significance today when we have again been at war and confronted with the problem of treating large numbers of battle casualties. My task today is therefore to survey the field of reconstructive surgery in relation to the treatment of those who have been wounded in this war.

TREATMENT IN ZONE OF COMBAT

From all reports, there can be no doubt that the wounded are receiving better medical care than ever before. This is reflected in some of the figures that have been received, for example, there has been a mortality rate of less than 3.5 per cent among those who reach the hospitals at the front, a recovery rate of 75 per cent for penetrating wounds of the abdomen, and one of 80 per cent for penetrating wounds of the chest.

There are three principal factors that contributed to these results. The first of these — and the chief one, in my opinion — is that proper surgical treatment has been made available much closer to the front than ever before. Field operating hospitals are set up alongside the divisional dressing stations, and all casualties requiring immediate surgical procedures receive them without delay. The second factor is the better and earlier treatment of shock. Undoubtedly little could be done if huge stores of plasma were not available on the spot, but on the other hand, plasma would not accomplish the task if we had not learned how to make the best use of it. Although plasma is good, whole blood is even better, but because of the necessity of typing and cross matching, it is less adaptable to field use. The procurement and delivery of whole blood at the front so that it may be used within the prescribed time period of ten days after it is drawn presented great difficulties, but thanks to fine teamwork between the Army and the American Red Cross and to the miracle of rapid transportation by the airplane, they have been solved. In addition

to plasma and whole blood, human albumin and all types of intravenous solutions are available when needed. The conquest of shock among the wounded makes possible earlier and more effective surgical procedures, which in turn help to overcome infection, the second of the twin bugaboos of the military surgeon.

The chief injury in approximately 60 per cent of the wounded is one or more compound fractures. There is generally extensive comminution of the fragments, and often loss of bone substance. There is also severe damage of the soft tissue, including muscle and skin, and not infrequently injury of important nerves. Metallic fragments from explosive missiles or rifle or machine-gun bullets are driven into the soft tissues, where they constitute foreign bodies, carrying with them bits of soiled clothing and débris, including earth, gravel and rubble.

The immediate problem in the treatment of these wounds is the prevention of infection, and here too progress has been made. It is known that early and careful débridement with excision of all contaminated and devitalized tissue and the removal of gross foreign bodies — but with due regard to the preservation of viable bone fragments and important soft structures — goes far toward preventing serious infection. The wounds are left open, lightly packed with plain or vaseline gauze and covered with gauze dressings, and the limbs are then splinted. The closed plaster cast, always split after it is applied, with or without traction by means of adhesive plaster strips whose ends are fastened to the plaster or by skeletal pins incorporated in the plaster, is still the method of choice for splinting and evacuating.

The role of chemotherapy in the prevention of wound infection at the front is still debatable. All the evidence collected by the Subcommittee on Infected Wounds of the National Research Council has tended to belittle the effectiveness of the sulfonamide drugs when used locally in wounds. When placed in an open wound at the time of débridement in cases in which renewal is not possible because of the plaster-of-Paris covering, their effect, if any, is so transient as not to be worth while. On the other hand, there is no dispute about their effectiveness when administered orally in combating the spread of certain organisms, chiefly streptococci and anaerobic gas-producing bacilli. But they may be dangerous when given without checkup by laboratory tests, and such control is frequently impossible near the front. On the whole, it seems

*Presented at the annual meeting of the New Hampshire Medical Society, Manchester, May 15, 1945.
 †Owing to the absence of Dr. Wilson this paper was read by Dr. John Kopf of New York City.
 ‡Surgeon-in-chief, Hospital for Special Surgery, New York City.

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I have discussed the treatment of the wounded at the front, particularly that of those with compound fractures, because the results of such treatment have a great bearing on the reconstructive surgery that must be done later. The same also applies to the intermediate treatment that is carried on in the general hospitals located in safe areas behind the front, to which the wounded are evacuated following primary treatment. A great contribution to their better care has been made by the improvements in transportation and the wider use of the airplane. These make their evacuation quicker and safer.

The function of these hospitals is to provide medical care of the wounded until they are able to return to active duty or, if it is decided that they cannot be so returned, until they are in sufficiently good condition to make the journey by airplane or ship to the United States. According to a directive of the Surgeon General of the Army, no reconstructive surgical operations are to be performed in foreign theaters of operation and all wounded who require such procedures must be returned to this country. Notwithstanding this limitation on their surgical activities, these hospitals are making important contributions to the treatment of the wounded.

All the patients with injuries involving the bones and joints are the responsibility of the orthopedic surgeons, and they have the task of dealing with infected, malunited and ununited fractures and with the injuries of the joints. So far as invasive infections are concerned, including those from the anaerobic gas-producing organisms or the hemolytic streptococci, these are less frequent and better controlled — by penicillin and the sulfonamide drugs — than was the case in the last war. But the gain in this direction has been counterbalanced by the

increase in severe compound and comminuted fractures of the lower extremities resulting from the extensive use of land mines. Unfortunately, many amputations must still be performed because of vascular injury, extreme structural damage or gas gangrene, but the indications for such mutilating operations are now better known and more quickly recognized than before, so that more lives are saved.

When patients with compound fractures or joint injuries are admitted to these hospitals in the rear, the first step is to remove the plaster casts in which they were transported and to apply traction, either by adhesive strips or when indicated by skeletal pins, in conjunction with suspension splints. Therefore, the surgical objective so far as the fracture is concerned is to secure the best possible alignment of the fragments and to maintain it until either bony union is obtained or the healing progresses sufficiently to permit encasement in plaster without danger of loss of position, thus permitting transportation to the United States.

But the splinting of the fracture is only one part of the management of these battle-incurred compound fractures, the other part is the treatment of the wounds. There has been quite a swing away from the closed plaster or Orr no-dressing technic that was so popular in the early days of the war. Doubtless this has been motivated partly by the development of more efficient methods of chemotherapy, but successful experiments with secondary wound closure have also played a part.

Experience has shown that when a wound is left open with bone fragments exposed in its depths, sooner or later secondary infection develops even when it was clean primarily. The best method of insurance against secondary infection is to seal the wound by a barrier of intact skin and soft tissue. Primary closure cannot be practiced at the field hospitals because of the danger that would be incurred in early evacuation. On the other hand, when the wounds of compound fractures have been thoroughly débrided and the fractures properly splinted, the patients reach the rear hospitals before infection has developed. Under these circumstances secondary closure by suture or by skin grafts may be attempted with little risk, especially when the patient is protected by the administration of sulfadiazine or penicillin. Experience shows that the earlier the closure is attempted the better are the results. The optimum time is from three to five days, but many successful closures have been obtained after longer periods. Preliminary reports indicate that successful results have been accomplished in 75 to 80 per cent of the cases, and that even when the result was a failure little or no harm to the patient resulted.

Some surgeons advocate internal fixation of the fragments by the use of steel bone plates at the time of the closure, but it is too early to evaluate this procedure. The transformation of compound,

potentially infected fractures into clean closed fractures is a major advance and carries immensely favorable implications for patients who may require surgical reconstruction

SURGICAL RECONSTRUCTION IN THE UNITED STATES

From this brief survey of the treatment of war injuries involving the bones and joints in the zone of combat and in the rear, certain conclusions may be drawn regarding the task of surgical reconstruction that must be done in the Army and Navy hospitals in the United States. These are the following. Patients will be returned to this country at an earlier period following injury than in the last war. They will arrive in better physical condition than in the last war. In a large number of cases—perhaps as many as 75 per cent—the wounds will be healed. Chronic bone infection is a less serious problem than in the last war, and when present better methods of treatment will be available to deal with it. Many of the patients will be ready for reconstructive surgery as soon as they reach this country, and the long periods of waiting previously required for clearing of infection are no longer necessary. There will be fewer cases of malaligned and malunited fractures than in the last war, and the percentage of cases requiring reconstructive surgery will be smaller.

With this optimistic prediction, which I hope will be substantiated by events, let me turn to a consideration of some of the more frequently encountered conditions that require surgical reconstruction, and the procedures that may be employed in their treatment.

CHRONIC BONE INFECTION

The presence of discharging sinuses with a history of a war wound and a compound fracture is always presumptive evidence of a focus of bone infection. Whether surgical eradication of the focus is to be advised depends on examination of the wound and study of the x-ray films. The introduction of a probe often demonstrates bare bone at the bottom of the sinus, or if this fails, the introduction of radio-opaque material and x-ray examination shows the course of the sinus and whether it connects with bone. Study of the x-ray films demonstrates the presence or absence of sequestrums and reveals whether there are infected cavities in the bone that must be cleared out to obtain healing. When the bone is dense, overexposed films sometimes aid considerably in evaluating the situation.

The question is frequently asked whether the administration of penicillin would not obtain healing in such cases and eliminate the need for surgical treatment. Certain investigators have shown that in cases of chronic bone infection the drug does not penetrate to the focus when given parenterally, and that when sequestrums are present it is not

effective when given locally in the sinus. Surgical removal of sequestrums and opening and saucerization of bone cavities are just as necessary as ever, but to obtain the best results penicillin should be administered both before and following operation. Under these conditions, many of the wounds with low-grade chronic infections may be closed primarily, or if this seems unwise they may be packed open and closed secondarily at the end of seven to ten days. Immobilization of the extremity, preferably in plaster of Paris, is of great importance in obtaining this result.

Recent studies have shown the value of a high-protein diet and adequate vitamins in promoting wound healing. One investigator has also called attention to a state of chronic surgical shock in many of these patients, which must be combated by the administration of plasma or whole blood. It is evidenced chiefly by a secondary anemia and a decreased blood volume, and may not be shown by the ordinary tests for hemoconcentration.

UNUNITED FRACTURES

Nonunion of fractures is a frequent problem following projectile injuries. Such fractures require prolonged immobilization, and patience is often rewarded by bony union without more radical treatment. In the lower extremity, the use of a brace that protects the fracture but allows weight-bearing on the extremity is often productive of good results. If the nonunion is complicated by the presence of infection, the eradication of the focus with healing of the sinuses is a necessary preliminary step to surgical reconstruction, and may in certain cases be followed by healing of the fracture without other intervention.

The distinction between delayed union and nonunion is often difficult to make, and in many cases must depend on the surgeon's conviction of being able to offer the patient greater certainty of a good result and of saving time by proceeding with a bone-grafting operation at once. When the fragments are well aligned and in good contact, a minimal delay of six months appears to be wise, and the delay should be longer if bone infection has only recently been eradicated. In the case of the lower extremity, a trial of a weight-bearing brace should have been made.

In the case of malaligned or displaced fractures with nonunion, there is justification for earlier surgical intervention, since correction of the deformity is desirable and the chance of obtaining union by conservative methods is small. The same is true in cases with loss of bone substance in which natural healing cannot be expected to take place. In such cases the only cause for delay is a history of recent infection.

In the last war, it was a general rule to delay reconstructive surgery until at least six months after complete healing of the wound. Even this

period proved too short in many cases and latent infection flared up, causing failure of the operation. With the present availability of penicillin and the protection against infection that can be obtained by its use preceding and following operation it seems unnecessary to wait for a period longer than three months when there is no clinical evidence of infection.

Loss of skin resulting in thin broad scars, particularly in the region of the tibia, frequently constitutes an obstacle to any operation on the bones. Generally it is the part of wisdom to turn such cases over to the plastic surgeon for excision of the scar and plastic repair, either by sliding or pedicle skin flaps, preliminary to attempts at bony reconstruction. This makes the task of reconstructive surgery easier and helps to ensure a good result.

So far as the operative procedure for overcoming nonunion is concerned, most orthopedic surgeons lean toward the on-lay graft, usually taken from the tibia, with fixation by metal screws of vitallium or stainless steel. The advantages of this procedure are that it obtains and maintains realignment of the fracture with rigid internal fixation and at the same time stimulates union through the application of the graft. When there is loss of bone substance however, and a gap must be bridged by the graft, the results by this method have not been encouraging. After an apparently good result, at the end of three months with union of the graft there is generally a fracture through the graft and nonunion is re-established. This is thought to be due to a resorptive process in the graft that results from the fact that little if any of the transplant survives as living bone and that the larger part must be revascularized, resorbed and replaced by living bone before final union is obtained. The graft is weakened during the stage of revascularization allowing fracture to occur with little or no violence.

Various methods of solving this problem have been tried. Those that have obtained the greatest measure of success are the double graft and, in the case of the tibia, the transplantation of the fibular shaft as a living bone graft. With the first of these methods double on-lay grafts are used and the space between the grafts is packed with chips of cancellous bone. There is increasing evidence that cancellous bone is more quickly revascularized and transformed into living bone than is cortical bone, and this procedure capitalizes on that observation. By the time the cortical grafts that maintain alignment and fixation are revascularized and weakened, there is every chance that the cancellous bone will have obtained union.

The fibula lends itself for use as a bone graft in the surgical repair of nonunion, because it can be spared without any functional loss, and also because it is a stout tubular bone and slowly undergoes revascularization and consequent weakening. In the case of nonunion of the tibia it may be used as

a living transplant by means of transference first of one end and then of the other, without interference with the blood supply of the bone. By utilization of these newer methods, some of the extremities that were formerly sacrificed and amputated as a result of continued bad results may now be saved as functioning members. But to obtain good results in some of these cases, long-continued supervision and brace protection are required.

MALUNITED FRACTURES

Although the level of fracture treatment is undoubtedly higher in this war than it was in the last owing in considerable part to the higher standards of surgical training in recent years compared with those of twenty-five years ago there are still a certain number of cases of complicated fractures that result in malunion. Although such results necessitate corrective operations, the matter of straightening a deformity of the long bones presents no great problem to the well trained orthopedic surgeon. If an open operation must be performed with an osteotomy, the modern trend is to employ internal fixation of a type that obtains rigid immobilization combined with excellent toleration by the tissues. This results in maintenance of alignment with the best assurance of rapid bony union and the shortest period of immobilization.

JOINT INJURIES

Joint injuries resulting from war wounds are generally of three types. The first consists of the penetration of a projectile of some type into a joint with minimal intra-articular damage. The result depends on how soon and how thoroughly surgical treatment can be applied. If the patient can be treated with good facilities within six to eight hours, the foreign bodies can be removed, the joint washed out and closed and chemotherapy started. This generally results in avoidance of infection and restoration of satisfactory function without requiring reconstructive surgery. The second type of injury is one in which the projectile causes such extensive comminution of the bone that no matter how well it is treated in the early period, the damage is too great to offer possibility of functional restoration. The third type is one that is complicated by the development of infection, and regardless of the extent of the primary bony damage results in loss of articular cartilage and, from the functional standpoint, in limited or painful movement or both.

Reconstructive surgery is generally required in the latter two conditions, and the surgeon is faced with the difficulty of choosing between arthrodesis, which aims at obtaining solid ankylosis of the joint, and some type of arthroplasty aimed at retaining or restoring movement without pain.

In the last twenty years considerable experience with these different procedures has been obtained, which helps the surgeon to make this important

decision with greater certainty than before. In general it may be concluded that in the case of the wrist, shoulder or ankle, ankylosing operations in good position give better and more certain results than does arthroplasty. In the case of the elbow, good movement and function can be expected to result from resection or arthroplasty, the latter procedure being reserved for those cases in which the normal bony structure is preserved.

In the case of an injured knee or hip, the decision depends to a considerable extent on the wishes of the patient and his determination to obtain functional restoration, and also on the surgeon's experience and his conclusions concerning the relative merits of the two procedures. Excellent results have been obtained from arthroplasty of the hip and knee, but they are less predictable and certain than are those from arthrodesis. On the other hand, it can always be explained to the patient that arthroplasty does not burn his last bridge and that if the result proves unsatisfactory, arthrodesis may still be done. In general, however, when the function of the other joints is normal, better results can be expected from arthrodesis than from arthroplasty.

QUADRICEPS MUSCLE LENGTHENING

One of the frequent complications of infected compound fractures of the femur following war injuries is fixation of the knee in extension. This is generally due to a combination of muscle damage and adherence of the quadriceps muscle to the femur, with loss of extensibility that prevents flexion of the knee. In 1919, Bennett¹ called attention to this condition and described a surgical procedure to lengthen the rectus tendon that resulted in restoration of function.

More recently Thompson² has described a new and simplified technic to obtain the same result. His procedure consists in isolating the rectus muscle and separating it from the vastus internus and externus muscle, and also from the intermedialis. When this is properly done, the knee can be flexed to an angle of 90° or better, and later by means of a program of exercise treatment excellent power of extension can be obtained. This may result in restoration of function in a knee that originally seemed hopelessly stiff.

NERVE INJURIES

Although nerve injuries are in the domain of the neurologic surgeon, they so frequently occur as accompaniments or complications of compound fractures that they also present problems for the orthopedic surgeon. Generally in such cases it is the best policy to clear up infection and obtain union of the fracture before attempting to repair the nerve. No neurologic surgeon is willing to mobilize and suture the nerve ends until wound healing has been obtained, and recovery of nerve

function does not improve the condition of the patient until union of the fracture has been brought about. During this long period the paralyzed extremity must be supported by splints to prevent contracture of the normal unparalyzed muscles, and active and passive exercises should be carried out to maintain mobility of the joints.

Interesting studies on nerve repair have been made during this war, and these have resulted in the development of such new methods as the use of plasma glue and of tantalum wire and of the envelopment of the repaired nerve ends with tantalum foil, each of which is thought to represent an improvement on old methods. The value of nerve grafts, whether fresh or frozen, is still debatable, but the experience of this war ought to provide an answer to this question for all time.

Nor should it be overlooked that in case of failure to obtain repair of an injured radial nerve the orthopedic surgeon can offer an excellent substitute in the form of tendon transplantation, and also in the case of irreparable injury of the common peroneal nerve, in the form of arthrodesis of the subastragalar and midtarsal joints, with transplantation of the posterior tibial tendon to correct the drop-foot and varus deformity.

AMPUTATIONS

Although an amputation is always a mutilating operation, it may at times be a reconstructive procedure in that the artificial limb permits better function than would the crippled extremity. In most cases, however, an amputation is done as a life-saving procedure, and unfortunately in the treatment of war casualties it must frequently be resorted to. But the problem of future rehabilitation is intimately related to every amputation that is performed, and it is of the greatest importance to see to it that a stump is produced that is capable of wearing an artificial limb with comfort and of giving the patient maximal function.

As in the last war, amputations in the combat zone are being done by the guillotine method through the site of fracture, since this procedure saves the maximum length of stump and best deals with the problem of infection. The method requires continuous traction to the skin in the postoperative period. This is obtained through the application either of adhesive strips or of stockinette glued to the skin. When the operation is correctly done and the proper aftertreatment is employed, the results are astonishingly good. Healing generally occurs in six to eight weeks, complications are few, and many of the stumps, particularly in the case of the thigh and of the upper extremity, require no additional surgery. In the cases that have unsatisfactory and adherent scars, the secondary procedure is of minimal severity and consists of excision of the scar, mobilization of skin flaps and simple closure. Reamputation is required only in the case

of long below-knee stumps, and resection of bone only when there is infection

Treatment of amputation stumps in this country is concentrated in seven Army general hospitals and in two Navy hospitals, which have been designated as amputation centers. Orthopedic surgeons who are especially experienced in amputation surgery and the fitting of artificial limbs are in charge of these services and direct the work. Limb-fitting shops have been set up in these hospitals, and as soon as the stumps are ready artificial limbs are fitted.

The Army is supplying articulated legs made of wood fiber that are readily modified to meet individual needs and are proving highly satisfactory. These will serve as alternate limbs when the veterans are fitted with permanent limbs after discharge from the Army. Special facilities have been organized to help in the rehabilitation of these patients.

REHABILITATION

Finally, it should be pointed out that surgical reconstruction is only the first step along the path of recovery, and that a complete program of rehabilitation is required that ends only when the injured veteran has been replaced as a useful citizen in his community. Without this the finest surgery will fail to obtain satisfactory results.

Most of these men have undergone profound mental shock, and at the same time are confronted with social, family and economic problems that they feel unable to solve. They must be helped back to a healthy mental outlook, and here the services of a psychiatrist are necessary, helped by a competent social-service case worker who looks into the patient's family and social background and helps in solving the problems. Between them they help the patient to obtain a better social and psychological readjustment.

A program of physical reconditioning is required to build up strength in injured and atrophied muscles and to restore movement in stiffened joints. This should begin when the patient is still in bed, and should aim both at restoring function in the extremities or parts of extremities that can be exercised and at awakening interest in an apathetic mind. Both doctor and nurse can play important roles in helping to develop and institute such programs as early as possible. Physical therapy and occupational therapy can play important roles in the program, especially after the patient has become ambulatory. At a later stage, gymnastics, sports, shopwork and a good recreational program can play their part in helping to achieve the maximum of physical reconstruction.

Finally, after discharge from the military forces, if the veteran's injuries are of a nature to constitute an obstacle to his returning to his former occupation, he should be given vocational training based on aptitude tests and vocational counseling. Such

training should continue until the veteran has been placed on a job and has shown himself competent to hold it.

All these services are now available to the wounded veteran through the Army Navy and Veterans Administration. If they are utilized to their fullest extent, the future fate of these men will be far better than after the last war and we may look forward with confidence to their return to their own communities and resumption of their places as useful citizens.

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DISCUSSION

DR EZRA JONES, Manchester: I want to express my appreciation to the author of this paper for taking up so many important points. His instructions about treating osteomyelitis by penicillin without operative procedure, is extremely interesting. We have found that unless such lesions are open with all the dead tissue cleaned out, the results are not particularly good. But with operative procedure and penicillin, they are excellent.

DR ROBERT R. RIX, Manchester: It is probably safe to say that the most frequent cause of delayed union and nonunion is the lack of complete, prolonged, adequate immobilization of the fracture. In some cases, I am sure that immobilization is stopped before it should be stopped and then the fracture is called nonunion when actually it is only delayed union. The immobilization should be complete. The unpadded cast should probably be used more than it is. The first cast, of course, should be lightly padded for reasons of circulation, but a skin-tight plaster can soon be applied to give complete immobilization. Also, if one immobilizes the fracture and permits early function, the chances of union are much greater than they are if the fracture is mobilized early. In other words early function and prolonged immobilization are preferable to early mobilization and short periods of fixation.

DR JOHN KOFF (closing): I hope the impression has not been conveyed that we believe that these infections should be treated with penicillin alone and without surgery. Practically everyone agrees that where there is bone infection with a sequestrum or actual infection in scarred areas, penicillin merely enables the surgeon to do a better job and does not eliminate the use of surgery. What we plan to do in most cases is to treat these patients with penicillin for a few days or a week and then operate to remove the sequestrums or the infected areas, with early secondary closure. No doubt we all agree with Dr. Jones that penicillin alone cannot be relied on to clear up these infections, except in acute cases.

Dr. Rix brought up the question of nonunion. Most of us will agree that lack of adequate immobilization is an important factor, but that is not the only thing, other factors come into the picture. We all know that fractures of the surgical neck of the humerus heal no matter what is done to them, no matter how much motion there is, one practically never sees a nonunion of the surgical neck. Mobilization is more desirable in those cases for function of the shoulder. In the tibia and the fibula, however, where there is need for adequate immobilization, I quite agree that if adequate fixation is not obtained, — and I am sure Dr. Wilson would agree with this, — either with a bone plate or some other fixation, a nonpadded plaster has an important place. We use it a great deal, and I find more and more orthopedic surgeons and general surgeons who having tried it are using it earlier and earlier.

A friend of mine recently saw me putting on a nonpadded plaster five days after the fracture, and remarked that he put them on in the beginning. He said that if he saw the patient within an hour or two after the fracture, he put the plaster on immediately after examination. But he admits that he would not do that after five or six hours or two days.

MEDICAL PROGRESS

THE PATHOGENESIS OF RENAL INSUFFICIENCY*

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IN POPULAR usage, the expression "renal insufficiency" has come simply to mean renal failure to maintain chemical homeostasis. In a restricted sense, however, there may be many renal insufficiencies. The acid-base balance may be maintained, while nitrogen accumulates in the blood, and conversely, nitrogen excretion may be unaltered when acidosis and dehydration result from urinary loss of water and electrolytes. Water reabsorption, nitrogen excretion or sodium conservation may each be affected individually, but in most disorders of renal function and structure, renal dysfunctions and their sequelae are multiple. The discussion that follows is devoted to a consideration of the pathologic mechanisms by which these disturbances are produced.

DEFINITION OF UREMIA

In any discussion of renal insufficiency, the word "uremia" occurs again and again. Unfortunately, it lacks a final and widely accepted meaning, in large part because the growth of knowledge has wrought great changes in the concepts of renal disease. According to Fishberg,¹ the word was coined by Piorry in 1840 to designate the clinical state resulting from the "retention of urine in the blood." It is now recognized that losses of salt and water through the kidneys may contribute as heavily in the pathogenesis of the clinical syndrome as renal retention of metabolic waste products. Nonetheless, retention continues to be stressed in most authoritative definitions.¹⁻⁶ The clinical picture originally described has been shorn of those manifestations now known to be the effects of hypertension^{1, 2} (hypertensive encephalopathy), although popular usage often overlooks this fact. Finally, minor differences in meaning appear among the various authoritative definitions, the following samples of which will suffice to illustrate the points of general agreement.

"We characterize the clinical phenomena which occur exclusively with renal insufficiency as *true uremia*." Volhard.⁶

"Uremia designates only that symptom-complex which occurs in conjunction with and as a result of the retention in the blood of urinary waste products." Harrison and Mason.³

"Uremia — the symptom complex resulting from renal insufficiency and accompanying the retention of urinary constituents in the organism." Fishberg.¹

"Uremia — azotemia resulting from intrinsic renal disease." Goldring and Chasis.⁴

"Uremia is the clinical syndrome which marks the point at which renal insufficiency is advanced enough to alter the composition of body fluids, with resultant serious disturbance of bodily functions." Page and Corcoran.⁵

Although it is generally conceded that the term "uremia" should be used only with reference to renal failure due to intrinsic renal disease, it is often extremely difficult or impossible to differentiate primary renal disease from disorders of the kidney secondary to extrarenal factors. Pure cases of either type are uncommon, since renal damage often causes changes elsewhere in the body that may in turn produce further destruction of renal tissue, whereas contrariwise, renal functional disorders produced by such extrarenal processes as congestive heart failure, traumatic shock and dehydration may provoke, if long maintained, serious and irreversible renal parenchymal lesions. Consequently, in this communication, the word "uremia" denotes the clinical state associated with nitrogen retention and disturbances of body water due to renal insufficiency, regardless of etiology.

RENAL INSUFFICIENCY IN INTRINSIC RENAL DISEASE

Recent developments in the study of the renal structural and functional defects leading to insufficiency in chronic Bright's disease have been surveyed at length in a previous progress report.⁷ The present discussion is concerned with certain special aspects of the problem.

Glomerulotubular Imbalance

Glomeruli and tubules vary considerably in size and probably, therefore, in functional capacity. Evidence has been advanced recently to support the view that a balance exists throughout the kidney between the glomeruli and tubules such that the capacity of one matches the capacity of the other.^{8, 9} According to this concept, it is likely that in the normal kidney large glomeruli are attached to large tubules and small glomeruli to small tubules. With

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disease, this proportion is marred and the resulting imbalance appears to be responsible for many of the manifestations of renal insufficiency¹⁰. Thus, damage limited to the tubules results in an inability of the kidney to reabsorb efficiently the great volume of glomerular filtrate, body water and electrolytes are lost in large amounts, and death follows if restitutive processes, such as glomerular pressure reduction by afferent arteriolar constriction or by hypotension, do not come into action. On the other hand impairment of glomerular filtration alone may result in oliguria and even anuria, since healthy tubular tissue may continue to operate blindly on the small volume of filtrate, concentrating it and reabsorbing solutes.

The last situation appears in the so-called 'acute uremia' of organic renal diseases¹⁰. Here glomerular damage causes a reduction in filtration rate. In view of the fact that most nitrogenous substances in the urine pass through the glomerular filter, it is not surprising that nitrogen retention follows filtration reduction. Urea, making up the largest moiety of the plasma nonprotein nitrogen, is particularly affected because it appears to diffuse back into the blood in large amounts when the urine flow is reduced and urinary concentration is increased. Sodium chloride and water are likewise retained because the tubule cells have an improved opportunity for reabsorption from the retarded stream of tubular urine¹⁰. Water and salt retention lead to edema and increased plasma volume.

Once glomerulotubular balance is restored in glomerulonephritis the clinical picture improves. If healing does not follow, however imbalance may develop and produce the so-called "nephrotic syndrome". Although tubular damage is usually obvious histologically, the glomerulotubular imbalance in this instance is similar to that of acute diffuse glomerulonephritis, since water and salt retention appear. Glomerular damage in this state not only results in reduction of the filtration rate but also in the excessive loss of plasma protein. A general metabolic disturbance, manifested in hyperlipemia and hypercholesterolemia, may also be responsible for insufficient plasma-protein replacement¹¹. Hypoproteinemia, with loss of water into the tissues, probably causes, in effect, a concentration of the plasma, setting in motion the hypophyseal-hypothalamic-renal mechanisms through which urine is concentrated. In this way further retention of water results. Moreover, urea is excreted in smaller amounts, as a consequence of oliguria and impaired filtration. With sufficient glomerular damage azotemia may develop. In most cases of the nephrotic syndrome of chronic diffuse glomerulonephritis nitrogen retention is not significant. In intercapillary glomerulosclerosis, on the other hand, the nephrotic syndrome and uremia frequently coexist¹². The renal insufficiencies that develop on the basis of the contracted kidney of chronic renal disease

and of the extensive diffuse renal destruction of more acute disorders such as malignant nephrosclerosis and bilateral cortical necrosis, are quite similar in their clinical manifestations and underlying renal functional patterns¹³. In all, tubular damage is severe. The remaining glomeruli may be attached to nearly nonfunctional tubes, which act simply as conduits for the passage of more or less unchanged glomerular filtrate to the bladder. The overburdened tubules become, as it were, "permanently diuretic" they are sufficiently active to remove glucose from the small total volume of filtrate but not capable of sparing water and electrolytes. Impairment of the "obligatory" water reabsorption is revealed in the approach of the urea and inulin clearances toward equality¹⁴. These factors play an important role in the production of hyposthenuria and isosthenuria.

Hyposthenuria

The formation of hypotonic or hypertonic urine requires renal tubular development and utilization of energy for osmotic work. Quantitative analysis of the relation between renal work and urinary concentration reveals that the renal tubular cells are called on to do a minimum of osmotic work when the urinary specific gravity is limited close to or fixed at 1.010¹⁵. When hyposthenuria develops in the course of renal disease, it is generally assumed that tubular damage prevents efficient energy development. Consequently, the determination of the maximal urinary specific gravity has been advocated as a measure of the extent of parenchymal destruction. Doubt has been cast on this concept. Goldring and Chasis⁴ have observed normal urinary concentrating power in the midst of uremia due to malignant nephrosclerosis. Hyposthenuria frequently develops during shock at a time when no kidney damage is demonstrable. It is probable that other factors are concerned in establishing the maximal level of urinary specific gravity.

Hayman and his co-workers¹⁶ have studied this problem carefully. They found that reduction of tubular tissue by any method was followed by hyposthenuria. When, however, the residual tubular tissue was obviously normal, as after subtotal nephrectomy, concentrated urine was formed if the glomerular pressure and filtration rate were lowered by hypotension or by increased plasma oncotic pressure (following the administration of acacia). When tubular damage was diffuse, as in uranium nephritis, these measures did not restore the concentrating power. This work indicates that a glomerulotubular imbalance may be responsible for certain cases of hyposthenuria. In these, the residual tubular transfer mechanisms may remain in good order, but the shortened time of contact between the cells and the tubular urine, as a result of nephron diuresis, may provide no opportunity for their operation. In short, a failure of energy utiliza-

tion rather than a deficiency of energy production is responsible. The possibility that this factor may be concerned in conditions of severe and diffuse tubular damage has not been eliminated. Under these circumstances, a great reduction of filtration rate would be required to permit efficient operation of the residual normal transfer mechanisms.

On the whole, Hayman's work supports the concept that the maximal urinary specific gravity and the residual functional mass of kidney tissue are related in diffuse renal disease. In this situation, the determination of concentrating power remains a valid and useful test. Corcoran and Page,¹⁷ taking cognizance of the factors discussed above, have used the maximal specific gravity in devising an accurate clinical method of estimating tubular mass. According to these workers, the maximal specific gravity (*S G*) of the urine and the urea clearance (*Cu*), rough measures of glomerular filtration rate, are related as follows to the residual functional tubular mass (*T*), expressed in per cent

$$\frac{(S G) - 3.4}{2.58} \sqrt{Cu} = T$$

It is properly emphasized that this formulation is approximative and may be invalidated by severe renal disease or extrarenal factors.

Renal Reserve

It is remarkable that renal disease must be far advanced before its presence is manifested by nitrogen retention. This apparent failure of a correlation between functional capacity and maintenance of homeostasis by the kidney has been ascribed to the operation of the so-called "renal reserve." There is considerable evidence in favor of this notion.¹⁸ Underlying all discussions of reserve, however, is the assumption that intermittency of glomerular activity similar to that observed directly in the kidney of the frog¹⁹ occurs in man. Direct²⁰ and indirect⁹ evidence set forth in the past three years appears to have disproved this assumption. Other explanations must be sought for the phenomena previously ascribed to renal reserve. Much of the experimental work on dogs may be discounted because of trauma and anesthesia. In man, the lag in the development of azotemia as renal tissue is destroyed may be ascribed to two possible factors. First, protein intake is reduced by anorexia, a common symptom of chronic renal disease. Second, hyposthenuria and polyuria appear with progression of renal disease and result in more efficient excretion of urea. Of these alterations, the first is probably the more important since it has been shown that the blood-urea nitrogen concentration rises to a level commensurate with the urea clearance when urea is administered to patients with renal damage.⁴ Changes of urine flow in man under various circumstances have frequently been ascribed to changes in the number of functioning glomeruli, that is, a shift in the size

of the renal reserve. This explanation fails to take note of the fact that urine flow and glomerular filtration rate in man are not directly related. Urine flow may change through the widest possible range without any significant alteration in the rate of glomerular filtration. Moreover, it is gratuitous to seek a relation between the two in view of the extent to which filtrate volume exceeds urine volume. Sufficient evidence is at hand to support the view that urine flow is largely a function of tubular water reabsorption under the control of hypophyseal-hypothalamic humoral activity.

In many women who develop proteinuria and hypertension during pregnancy, signs of renal disease may clear completely during the puerperium. This syndrome may recur in subsequent pregnancies without permanent effect. It has been suggested that a congenitally small renal reserve may account for the clinical findings.²¹ The stress of pregnancy is assumed to evoke increased renal activity, of which the kidneys are incapable. Proteinuria and hypertension are then thought to develop as a result of renal stress. Since the fundamental premise of this concept appears to be in error, however, it seems likelier that the "low-reserve kidney" signifies a benign form of the specific toxemia of pregnancy. Functional studies of the kidney in normal pregnancy have revealed no significant changes in renal blood flow, glomerular filtration rate, or tubular activity that might be construed as evidence of a strain imposed by pregnancy.²² Indeed, it appears that pregnancy is not associated with detrimental renal functional change even when the kidneys have been damaged by essential hypertension or chronic diffuse glomerulonephritis, provided the specific toxemia of pregnancy does not supervene.²³

RENAL INSUFFICIENCY IN EXTRARENAL DISEASE

General Considerations

In a variety of illnesses, the signs and symptoms of renal insufficiency may appear in the absence of renal disease. The terms "prerenal azotemia" and "extrarenal uremia" have been applied to this state. In one respect these expressions are to be deplored because they divert attention from the kidney. It is true that extrarenal factors are primarily at fault and are to be dealt with therapeutically. Nonetheless, in the vast majority of cases, the renal dysfunction and damage are secondary and, in turn, cause nitrogen retention. In a small number, extrarenal factors of increased nitrogen intake or production give rise to azotemia.

The fundamental causes of impaired renal function in extrarenal uremia remain obscure, but recent work has thrown light on certain aspects of pathogenesis. Since peripheral circulatory collapse and dehydration are of common occurrence in all the conditions in which prerenal azotemia is seen, Fish-

berg²⁴ and others²⁵ claim that a renal circulatory defect lies at the bottom of most cases. Recent findings have strengthened their stand. The possibility remains, however, that alterations in plasma composition or nephrotoxins are responsible in many cases.

It has been widely held that hypochloremia may cause temporary, perhaps permanent, renal dysfunction. Hypochloremia is frequently associated with uremia, and it is difficult to produce uremia experimentally without reducing the plasma chloride concentration. It has been shown,²⁶ however, that hypochloremia may be induced in various ways without evidence of renal damage, provided plasma volume and osmotic pressure are sustained. Hiatt,²⁷ for example, succeeded in replacing as much as 70 per cent of the chloride ion by the nitrate ion, maintaining this state in dogs without ill effect for as long as three months.

It has been suggested that hyponatremia may be at fault because excess removal of the sodium ion always induces renal insufficiency.²⁸ Many studies have shown conclusively the vital relation between the sodium ion and the volume, hydrogen-ion concentration and osmotic pressure of the body fluids.²⁹⁻³² Since the kidney operates to maintain constancy of the composition of the plasma,³³ it is difficult to isolate the effect of salt depletion from that of dehydration. The balance between salt and water in the body, however, may be upset by low sodium intake, excess sweating and increased water intake. Under these circumstances, the chief phenomena referable to the loss of sodium are muscular spasm and slowed mentation.³⁰⁻³⁴ Nitrogen retention occurs as body water is lost under these circumstances, but the reduction in plasma volume and renal efficiency is held in check at a certain point beyond which marked hyponatremia must develop before further changes ensue.³⁰ It seems likely, therefore, that sodium loss per se cannot be implicated as the direct cause of renal functional change.

A complex series of reactions appears in response to the loss of body water and base. Fluid moves from the cells to the extracellular spaces, while the kidney excretes concentrated urine and operates selectively on the various electrolytes in the maintenance of normal plasma composition, often without regard for the total volume requirements of the body. Although the factors controlling plasma volume are far from clear, it appears that, so long as excess electrolyte loss is prevented, the volume is maintained relatively constant during water loss at the expense of the extravascular fluid³⁵, but when sodium and other ions are depleted, plasma volume decreases and peripheral circulatory failure develops. Dehydration, however, cannot be thought of solely in terms of the volume of extracellular fluid. Hypernatremia of the volume has been shown to cause death in respiratory failure, probably as a result of marked

cellular dehydration,³⁶ even when plasma volume is well maintained and circulation is adequate.³⁷ Under these circumstances, renal function is normal. When dehydration leads to a diminution both of the extracellular fluid and of the plasma volume, however, renal insufficiency becomes manifest, even before any evidence of shock is discernible.

The character of the demonstrable relation between dehydration, hypovolemia and impaired renal function is not clear. A reduction in renal blood flow and glomerular filtration rate as a result of active vasoconstriction has been found in such diverse states as orthostatic syncope,³⁸ chronic anemia,³⁹ traumatic shock⁴⁰ and Addison's disease,⁴¹ all of which are similar, chiefly, in a reduction of the effective circulating plasma volume. Arterial hypotension is probably responsible in certain cases, but the phenomenon may be observed in the absence of blood-pressure change.^{39, 41} The possibility of neurogenic mediation or of the action of humoral, endocrine or toxic agents cannot be entirely eliminated.

Toxins released by traumatic destruction of tissue, by the action of disease on the tissues or by microorganisms have been evoked at various times to account for the renal disturbances in extrarenal uremia. For the most part, the toxins in question have been purely hypothetical, their presence and action being posited on the basis of pathological findings, such as widespread focal necrotic lesions and renal tubular necrosis, after clinical manifestations of toxemia, such as high fever, prostration and coma. Certain specific agents have been implicated, however, particularly in traumatic shock and infection.

At this point it is necessary to consider how such toxins might affect renal function. It is often assumed that tubular damage by toxins is sufficient to account for azotemia and other manifestations of renal insufficiency, but this view is incomplete. If tubular dysfunction occurred alone, excess water and electrolytes might be lost, as in diabetes insipidus or Addison's disease, but the excretion of urea and most other substances would be unimpaired until changes in renal hemodynamics and filtration occurred. Hence, any view of extrarenal uremia as secondary to toxic renal damage must include interference with glomerular filtration in an important position. Tubular lesions contribute to the total picture but alone cannot produce it. A possible exception to this point of view is found in conditions in which toxic agents, such as mercury, uranium, sulfonamides and possibly "heme" pigments, are concentrated to dangerous levels in the tubular urine. Even here, however, it is interference with filtration by blockage of the tubules, by total nephron destruction or by other mechanisms that leads ultimately to nitrogen retention and uremia.

Disorganization of renal functional activities is a constant factor in all the conditions to be discussed

below The considerations set forth above with respect to glomerulotubular imbalance in intrinsic renal disease hold force here Impairment of filtration rate greater than that of tubular function may lead to the excretion of a highly concentrated urine in small amounts In most cases, however, tubular dysfunction appears to be profound and a dilute acid urine is formed, often in normal daily volumes Since the urine is derived from a greatly decreased filtration bed, nitrogen excretion remains impaired despite the normal or even high urine flow Hyposthenuria under these circumstances, however, may not necessarily indicate tubular damage If the over-all filtration rate is reduced as a result of complete cessation of activity in a sufficient number of glomeruli, hyperfiltration in the remaining functional units may result in the formation of dilute urine

Peripheral Circulatory Collapse

It is well known that shock following trauma, blood loss, burns and the like is associated with a serious derangement of renal function manifested in oliguria or anuria, excretion of a dilute acid urine and nitrogen retention It is less well known that this disorder of renal function may persist even after recovery from shock, ultimately leading to death in uremia Cases such as those reported by Husfeldt and Bjerling,⁴² by Darmady and his co-workers⁴³ and others⁴⁴⁻⁴⁶ are unusual in civilian practice In combat areas, so-called "traumatic uremia" has been seen more frequently both because shock is frequent and severe and because treatment is often delayed Darmady et al⁴³ found that one third of their fatalities at an air-evacuation hospital in England were of this nature Six severely injured men in whom crushing injury was not a factor died in uremia four to seventeen days after injury and recovery from shock

The renal pathology of traumatic uremia varies remarkably from minimal cloudy swelling of the tubular cells, to extensive bilateral cortical necrosis^{42, 43, 47, 48} In general, the kidneys are enlarged and edematous The glomeruli may be bloodless or show changes resembling those of acute diffuse glomerulonephritis⁴² Degenerative changes of the tubular cells are usually prominent These lesions range from lipoid infiltration to necrosis There may be focal nephron destruction, tubular blockage by casts or tubular disruption As a rule, the pathological picture is best described as a nephrosis

Renal function during traumatic, burn and hemorrhagic shock in man⁴⁰ and animals^{49, 50} has been studied intensively in recent years as a result of the stimulus of war In the dog, episodes of hemorrhage sufficient to produce hypotension are at first easily reversible by transfusion but, if repeated frequently and quickly enough, lead to irreversible shock⁴⁹ Renal blood flow, also, is at first easily returned to a normal level by transfusion, but after the second or third bleeding, undergoes protracted reduction and

fails to recover after transfusion This phenomenon precedes the development of irreversible peripheral circulatory collapse In man, renal blood flow is nearly always markedly decreased during shock⁴⁹ Transfusion results in prompt recovery of blood pressure and cardiac output in most cases, but the renal circulation does not improve proportionately owing to active vasoconstriction within the kidney A similar vasoconstrictive response in dogs occurs even when the kidney is denervated or is under the influence of a sympathicolytic agent (933F)⁴⁹ These facts indicate that a vasoconstrictive humoral agent that does not act on the sympathetic nervous system may be responsible It has been suggested that increased renin production occurs in shock,^{51, 52} perhaps as a defense measure, but the only vasoconstrictor substance Page⁵³ could find in the blood of shocked animals did not behave like angiotonin Indeed, it appears that the vascular system becomes refractory to angiotonin following hemorrhage or extensive central nervous system trauma⁵² Other workers⁵⁴ have also failed to find evidence that the renal pressor system is active in shock

Since approximately 25 per cent of the cardiac output pours into the kidney normally,³⁸ renal vasoconstriction during shock effectively diverts a significant mass of blood to more vital organs A similar buffering circulatory activity of the kidney has been found normally present and highly developed in certain animals The seal, for example, can endure long periods of asphyxia during diving, in part because blood is diverted to the heart and brain from the kidney by intense vasoconstriction⁵⁵ In man, it may be that a similar normal activity of the kidney (if maintained too long by shock) is detrimental and irreversible Penner and Bernheim⁴⁷ have shown that intense renal vasoconstriction, if sufficiently prolonged, causes bilateral cortical necrosis, a disorder they and others⁴⁸ have observed following shock

On the other hand, vasoconstrictive toxins released from traumatized tissues may be at fault in evoking a pathologic response The hypothesis that the entire shock state is produced by circulating toxins has long had wide support⁵⁶ At the close of World War I, this hypothesis was generally held to be well founded as a result of the extensive work of Cannon⁵⁷ and others Subsequent work⁵⁸ has discredited certain of the major premises of the toxemia theory,⁵⁸ and the view that the reduced plasma volume of shock is secondary to local fluid loss rather than to a generalized loss through toxin-damaged capillaries has gained strength Facts have emerged recently, however, that appear to give some weight to the toxemia theory A number of workers⁵⁹⁻⁶² have shown that a toxic substance may appear in lymph draining from crushed or traumatized regions or in the blood during circulatory collapse Moreover, it has been claimed that bacterial toxins arising from anaerobic bacterial growth in macerated tissues

may be responsible.^{63, 64} Although the latter finding casts doubt on the validity of much of the evidence for a toxin in muscle extracts, there is good reason to believe that pigments and possibly other substances released from damaged muscular tissue may be responsible for the profound renal damage of the "crush syndrome."

In 1941, Bywaters and Beall⁶⁵ described the "crush syndrome" observed following prolonged compression and crushing of muscles in victims of the air war over London in the fall of 1940. Their observations have been repeatedly confirmed, and a large number of additional cases have been reported. Severe shock apparently always develops after such an injury and usually responds to treatment. Following recovery from shock, clinical evidence of renal insufficiency appears and death in uremia occurs in about eight days. Myohemoglobin and creatine appear in the urine in large amounts shortly after release of the compressed part, and it has been suggested that myohemoglobin may have a nephrotoxic action.⁶⁶ Pathologically, the renal lesion resembles that of shock. The tubules are markedly damaged. Necrosis with fragmentation and blockage by brown granular casts are particularly prominent in the distal segments.⁶⁶ The casts appear to be precipitated myohemoglobin.⁶⁷ Other states in which "heme" pigments are free in the blood, such as blackwater fever,⁶⁸ transfusion reactions⁶⁹ and spontaneous myohemoglobinuria,⁷⁰ may also be complicated by renal failure. A similar lesion has been produced in acidotic dogs with canine methemoglobin.⁷¹ Bywaters and Stead,⁷² also, found acidosis requisite for the production of tubular lesions in rabbits with human myohemoglobin. It is unlikely that methemoglobin is involved in man, since this substance may occur free in the blood without effect⁷³ and does not appear in the urine of patients with traumatic shock or the crush syndrome.⁷¹ Whether shock is necessary in the production of the crush syndrome in man is not clear.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 31431

PRESENTATION OF CASE

A thirty-five-year-old woman entered the hospital complaining of a limp in the right leg.

Eight months before admission, while walking downstairs, she felt her right hip suddenly give way simultaneously with a sensation of numbness and tingling in the right heel. During the following night a black-and-blue area developed on the posterior aspect of the thigh, spreading downward to the mid-calf. There was no pain at any time. At a community hospital she was placed in a spica. After eight weeks the cast was removed and the patient walked with crutches. Limitation of flexion of the right knee was noticed for the first time. A month later she began to walk without crutches. There was no pain in the hip, but the right leg remained swollen and heavy, and she limped.

Twelve years before admission the patient was exposed to syphilis but noted no primary or secondary lesions. Ten years later she had a blood test and

*On leave of absence.

was then given weekly hip injections for two and a half years. There was no history of headache, vertigo, paresthesia, shooting pains or visual disturbance.

Physical examination revealed a well developed and well nourished woman in no distress. The pupils were irregular, the right being slightly larger than the left and reacting less to light than the left, both reacted to accommodation. The heart and lungs were negative. The right lower extremity was 2.5 cm shorter than the left. The right upper thigh was firm and swollen. The right hip showed a permanent flexion of 50°, but further flexion to 80° was possible. The extremity was externally rotated. There was no internal rotation of the thigh on flexion or extension. External rotation was 30° on flexion. Abduction was 25°. Extension of the knee was normal. Flexion of the knee was possible to 150°, with painless catching. The left patellar and Achilles tendon reflexes were slightly hyperactive, those on the right were present and normal. There was no clonus or Babinski sign. Position sense was normal. The visual fields were normal.

The blood pressure was 135 systolic, 85 diastolic. The temperature was 99°F, the pulse 80, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,750,000, with 80 per cent hemoglobin, and a white-cell count of 15,000, with 68 per cent neutrophils. The urine gave a + test for albumin, and the sediment contained 25 red cells and 10 white cells per high-power field. The serum calcium was 9.6 mg per 100 cc, the phosphorus 2.9 mg, and the alkaline phosphatase 8.5 units. Blood Hinton and Wassermann reactions were positive. The spinal-

fluid Wassermann was negative, as was the gold-sol curve. The spinal-fluid protein was 22 mg per 100 cc.

An x-ray film of the chest revealed no lesions in the lung or bones. The right knee showed decalcification of the bones, but the joint appeared normal. The right thigh showed a transverse fracture of the neck of the femur (Fig. 1). The greater trochanter

tion in its substance. The periosteum was lifted for some distance below this large calcific mass.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CHANNING C. SIMMONS: We might as well see the x-ray films first.

DR. CLAYTON H. HALE: These films, taken at



FIGURE 1. Roentgenogram of the Right Hip Taken Eight Months after the Initial Injury.

was displaced upward and somewhat laterally. A large laminated, calcific mass, irregular in outline, surrounded the lower neck and the upper half of the shaft. The mass was somewhat less calcified in the region immediately adjacent to the shaft and in the region of and distal to the trochanter. The outline of the femur was irregular and somewhat moth-eaten, and there were multiple areas of decalcifica-

tion in its substance. The periosteum was lifted for some distance below this large calcific mass. An operation was performed.

DR. CHANNING C. SIMMONS: We might as well see the x-ray films first.

DR. CLAYTON H. HALE: These films, taken at

right after the accident, and there would not have been time to lay down that amount of calcium. These later films were taken here, and they show considerably more of this calcified material lying out in the soft tissue, they suggest the appearance of nonunion, which one might also see with pathologic fracture. The density is well rounded off in this area, and one surely must think of a Charcot joint.

DR SIMMONS But you would expect it to be more in the joint, would you not?

DR HALE Yes, that is the usual thing.

These films were taken after the patient came here. The material in the soft tissue has become organized and shows an attempt at early bone formation. You can see periosteal calcification here, and evidence of metallic material in the buttock.

DR SIMMONS The discussion of any of these bone diseases comes down to a consideration of conditions under three headings: general systemic disease, such as tuberculosis and syphilis, skeletal disease, such as osteitis fibrosa cystica and Paget's disease, and bone tumors, benign and malignant, primary and metastatic.

Regarding systemic diseases, what data we have rule out tuberculosis. Syphilis always has to be considered. This is not a typical Charcot joint because it is not in the joint, and it is not the characteristic picture of syphilis of the bone. I do not believe, however, that there is a characteristic picture of syphilis of bone. There is the one that is most frequently seen, but about anything can be observed.

The systemic disease to consider here is Paget's disease. The patient was rather young for that—thirty-five years. We have no other films of bones with which to compare these films, but there is nothing to suggest Paget's disease, nor is there anything to suggest osteitis fibrosa cystica.

We are left with the consideration of some form of bone tumor or a traumatic condition, keeping the reservation of possible syphilis. The patient presumably had a pathologic fracture, that is, the leg collapsed while she was going downstairs. Spontaneous fracture of the neck of the femur may occur in an elderly person, but one would hardly expect it to occur in a person of thirty-five, therefore, a pathologic fracture seems likely. None of the films taken at the time of injury are satisfactory (Fig 2). All are rather hazy, but one can see some bone formation around the area. The joint looks normal. I do not know exactly how soon after the accident the films were taken, but one would not expect, as Dr Hale has said, to see new-bone formation in the hematoma. There is also definite evidence of a progressive condition.

I believe that this is probably some form of bone tumor. We have nothing to suggest that she had a primary lesion elsewhere, except possibly the albumin and few red cells and pus in the urine, which, of course, might have come from the bladder or

from a vaginal discharge. There is no record of an examination of the abdomen, so we do not know whether she had a primary tumor of the kidney with metastases to the bone, the metastases having given the first symptoms. The blood examination is informative, since the phosphorus and calcium were normal and the phosphatase was elevated. One expects an elevated phosphatase in any process in which there is as much new-bone formation as there was here. An organizing hematoma raises the phosphatase. An osteogenic sarcoma also raises it,

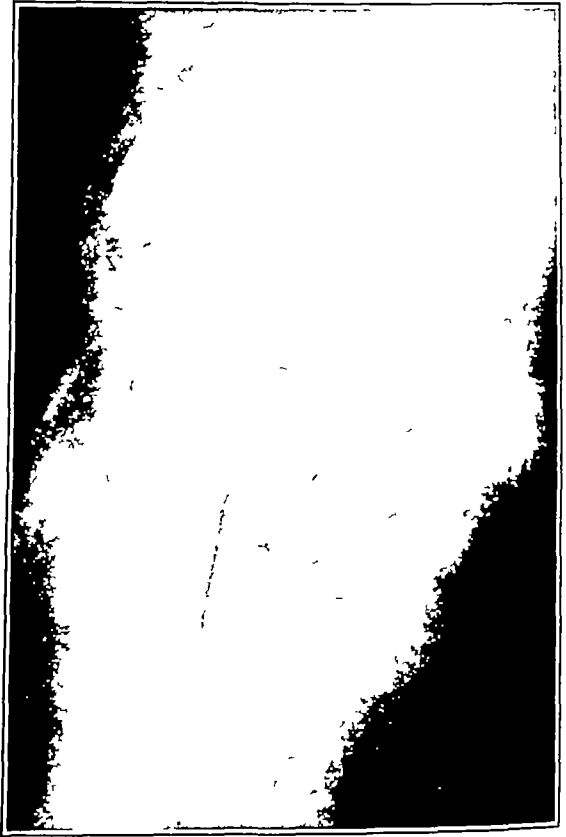


FIGURE 2 Roentgenogram of the Right Hip Taken at the Time of Injury

whereas an Ewing's tumor rarely has any effect. The serum protein level is not given, but in plasma-cell myeloma the serum protein is usually elevated. Plasma-cell myeloma, however, is a bone-destructive lesion, and there is nothing in the x-ray films to suggest that. Of the primary tumors of bone, benign and malignant, the malignant ones usually come at a somewhat earlier age than this, but any tumor, with the possible exception of chondroma or chondrosarcoma, which I prefer to call osteogenic sarcoma of the chondral type, is often found in people of sixty to seventy.

These first films do not show much. The patient obviously had something that weakened the bone. She could have had a chondroma of the bone that weakened it and caused it to collapse, with new-

bone formation. I believe that an osteochondrosarcoma is the most plausible diagnosis in this case always reserving syphilis. There is irregular bone formation, and in this there is ray formation of bone, which is probably coming down under the periosteum with new-bone formation and bone destruction at the same time. It is difficult to say whether tumor is superimposed over the neck of the femur. An osteochondrosarcoma, if you want to call it that, is a low-grade sarcoma; if treated relatively early, it can usually be cured by total removal. It is not a radiosensitive tumor.

DR. DAVID WILLIAMS: The operation was a biopsy. There were ray formation and new bone in the lateral and lower aspects of the mass, as one would

PATHOLOGICAL DISCUSSION

DR. SNIFFEN: My remarks on this case are a little anticlimactic. The biopsy consisted of a generous fragment of the calcific mass and a layer of overlying soft tissue. The mass consisted of bone trabeculae with pronounced osteoblastic activity in some areas and minimal activity in others. Osteoclasts were also present, but in relatively small numbers. The intertrabecular spaces contained a few fibroblasts and small groups of fat cells but were occupied for the most part by innumerable channels of varying diameter. Some of these were obviously blood vessels, but the majority contained fluid and granular precipitate, and their walls seemed to consist of a fine membrane of connective tissue without



FIGURE 5. A Photomicrograph of the Calcific Mass Showing the Bone Trabeculae and the Cystic Space.

expect from the x-ray. There was nothing else remarkable, and we had no other clue.

DR. RONALD C. SNIFFEN: Do you know the opinion of the other members of the service?

DR. WILLIAMS: We were all completely at sea.

CLINICAL DIAGNOSIS

Tumor of femur?

DR. SIMMONS'S DIAGNOSIS

Osteochondroma or osteogenic sarcoma (chondral type) of relatively low malignancy.

ANATOMICAL DIAGNOSIS

Multiple cysts of femur?

Excessive callous formation?

an endothelial lining (Fig. 3). This is reminiscent of what is seen in the cortical shell of a solitary bone cyst. In the layer of overlying soft tissue there was a surprising degree of endarteritis.

We cannot make a diagnosis, but if it is presumed that this biopsy is representative of the mass as a whole, various conditions can be ruled out, such as malignant tumor, giant-cell tumor, fibrous dysplasia, and osteomyelitis. There was no evidence of syphilis, and I can find no reference to such changes in a Charcot joint, either in the pre-ataxic stage or in the ataxic stage. There was no indication of an organizing hematoma. Perhaps the process is merely excessive callous formation.

In spite of our dilemma the patient is well. She has no pain and is walking without aid. It is now ten months after the fracture.

CASE 31432

PRESENTATION OF CASE

A fifteen-year-old boy entered the hospital complaining of pain in the left biceps muscle.

After an attack of scarlet fever three years before admission, he noted the gradual development of intermittent stabbing pain in the left biceps muscle, made worse by use of the muscle. There was occasional radiation of pain and numbness to the left hand. A year before admission weakness of the left arm appeared and progressed, and the muscle pain became extremely severe.

The past history was noncontributory.

Physical examination revealed a well developed and well nourished boy. The heart and lungs were normal. The spine showed left dorsal scoliosis, with winging of the scapulas. The left arm was atrophic and weak, especially about the elbow, with weakness also of the wrist and hand. The left triceps and radial reflexes were weaker than those in the right, and the left biceps reflex was questionable. The left biceps muscle was tender. When its strength was being tested by pull against it, the patient complained of pain in the muscle, which radiated down the ventral aspect of the forearm into all the fingers. During an attack of such pain an area of hypesthesia to pinprick appeared in the medial portion of the volar aspect of the left forearm. This lack of sensation lasted a short time, and in the absence of pain, hypesthesia was also absent. The skin of the left hand was more wrinkled and moist than that of the right. On electromyography, the only abnormal finding was hyperirritability of the extensor carpi radialis.

The temperature was 98.6°F, the pulse 70, and the respirations 15. The blood pressure was 125 systolic, 75 diastolic.

Examination of the blood revealed a hemoglobin of 12.8 gm. and a white-cell count of 8200, with 68 per cent neutrophils. The urine was normal. The blood chemical and spinal-fluid findings were negative. An x-ray film of the left shoulder region showed loss of the lordotic curve of the cervical spine, with evidence of spur formation about the margins of the vertebrae. The joint spaces were of normal width. The visualized bones about the left shoulder joint and the proximal portion of the humerus were normal. In the distal third of the humerus there was widening of the cortex in its medial portion, with a somewhat irregular and indefinite area of increased density, as well as central rarefaction extending out from the medullary canal (Fig 1).

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CARROLL B. LARSON. This is a good example of how a great number of facts regarding a history and examination are put together without following any of them to their actual termination, so that they

have some value. All sorts of conditions are suggested by the history, both neurologic and orthopedic. For example, although the record does not definitely say so, some of the neurologic findings suggest that there may have been injury to the cer-

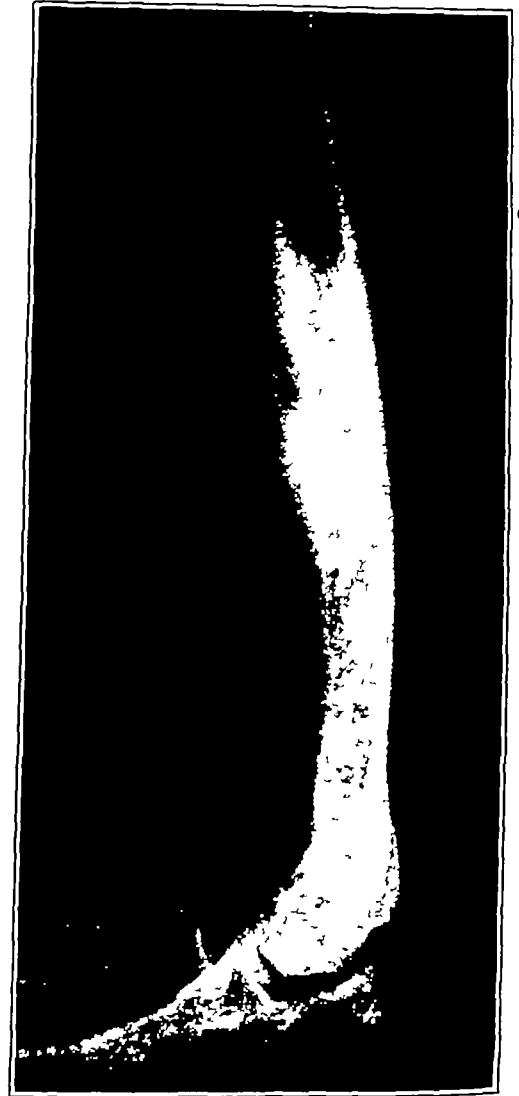


FIGURE 1. Roentgenogram of the Humerus, Showing the Area of Rarefaction Surrounded by Dense New-Bone Formation.

vical spine, yet it does not tell what the motions of the cervical spine were, to help rule it in or out.

Another point of interest is the tender biceps muscle. A muscle can be tender in many ways. If you push from front to back on the biceps muscle you may be eliciting tenderness on the underlying bone, but if you squeeze the muscle and find that it is tender, it means something entirely different. It is an important point.

The neurologic points registered here involve components of both the radial and ulnar nerves, and if one went into the realm of peripheral nerve lesions one would have to consider lesions involving more

than one nerve simultaneously, and roots at more than one level. All in all I think that the history and examination are of little help in trying to establish a diagnosis. Take an isolated fact, that of tenderness in the biceps muscle, and assume that the pressure was from front to back, which is the most frequent way in which tenderness is tested. If that was true, it might have elicited tenderness in the underlying bone. Or, by using the biceps muscle along with the brachial muscles, because they go together, the patient may have been pulling on some sensitive periosteal attachments overlying a bone lesion. We know perfectly well that in bone disease many vague patterns of nerve distribution pain may be elicited. They defy explanation of how they occur, whether reflexly or otherwise. Because this is a vague story of nerve distribution, one might conjecture that the lesion was in the shaft of the humerus, and that the pain elicited was from muscle pull on the sensitive area.

May we see the x-ray films?

DR. CLAYTON H. HALE: These films show the marked cortical thickening and the central area of rarefaction that were described. The latter looks almost like two cystic areas. I cannot make out any soft-tissue mass. One must think of a chronic low-grade inflammatory process as the likeliest diagnosis from the x-ray point of view.

DR. LARSON: There is a definite area of decreased density in the middle of a very dense orderly arrangement of periosteal new-bone formation. This x-ray appearance, disregarding the clinical points entirely, strongly suggests three possibilities — cortical abscess of bone, Garré's sclerosing osteomyelitis and osteoid osteoma. Garré's osteomyelitis, however, can be eliminated, because there is no focal point in this condition. Furthermore, Garré's disease usually involves the entire circumference of the shaft. For a cortical bone abscess, this, again, is not a characteristic x-ray picture, because when there is irritation from a point of infection in bone, one is apt to observe surrounding density as much on one side of the abscess as on the other. The area of decreased density lies next to the medullary cavity, and on that side there is little new-bone formation, except for a shell. In cortical abscess of bone I should expect the bone reaction to be more symmetrically divided on both sides of the lesion than it is here. This obviously has been going on a long time, because of the orderly arrangement of the periosteal new bone. One would not expect it to be a rapidly growing tumor, for in such cases there is a disorderly arrangement of bone formation.

The third possibility, which is by far the strongest, is that of osteoid osteoma. The cause of osteoid osteoma, whether infection or true tumor, is unknown, but regardless of that, this presents what we consider to be the characteristic x-ray picture of osteoid osteoma, that is, an orderly arrangement of periosteal new-bone formation, which is more or

less a reaction to a foreign substance, whether it be tumor or infection. Reaction is likelier to occur on the periosteal side of the bone, with only little reaction of the medullary side. This fits the picture of osteoid osteoma extremely well. I should have liked to know from the history more about the character of the pain. A severe deep bone ache is almost typical of osteoid osteoma. Furthermore, I should also have liked to know whether direct bone pressure on the lesion by the examining finger produced pain, because pressure over one of these areas intensifies the original pain. If that had been noted, one could suspect that diagnosis on the clinical aspect without waiting for the x-ray studies. I believe that this was probably an osteoid osteoma.

DR. EARL GLENDY: What about the x-ray films of the cervical spine that are recorded as showing evidence of spur formation at the margins of the vertebrae? Is that not unusual for a boy of fifteen years?

DR. HALE: The only film that we have is an anteroposterior one that does not show the spurs mentioned in the report. I can see nothing abnormal on this film. I am sure there were other films.

DR. CHANNING C. SIMMONS: The possibility of syphilis always has to be considered. I do not believe it is syphilis, but because of the thickened periosteum of the bone one should keep it in mind.

DR. RONALD C. SNIFFEN: What was your impression at operation, Dr. Williams?

DR. DAVID WILLIAMS: We did not know what it was. We thought that it might have been an osteoid osteoma because of the swelling. It was difficult to find the area of rarefaction. There was no pus. There was a definite cavity containing granular crumbling bone, which was weaker than the surrounding bone. The cortex was quite brittle, more than one might normally expect. A culture was taken from the area, and it was cleaned out, nothing further was done.

DR. SIMMONS: Were the symptoms relieved?

DR. WILLIAMS: The boy has been completely relieved and was discharged five weeks after operation. We have seen him once since then.

CLINICAL DIAGNOSIS

Osteoid osteoma of humerus?

DR. LARSON'S DIAGNOSIS

Osteoid osteoma of humerus

ANATOMICAL DIAGNOSIS

Osteoid osteoma of humerus

PATHOLOGICAL DISCUSSION

DR. SNIFFEN: Microscopic sections of the lesion showed fragments of extremely cellular, vascular connective tissue, and in this, osteoid trabeculae

were embedded (Fig 2) These trabeculae were lined by osteoblasts and occasional osteoclasts The trabeculae of the adjacent spongy bone were thickened, and the marrow fibrous There was no inflammatory infiltration or evidence of degeneration

important to know where it is, because you will not cure the patient unless it is removed By varying the x-ray technic in spot films, you may be able to demonstrate the nidus This is the same bone with a variation in the technic, it shows where the nidus

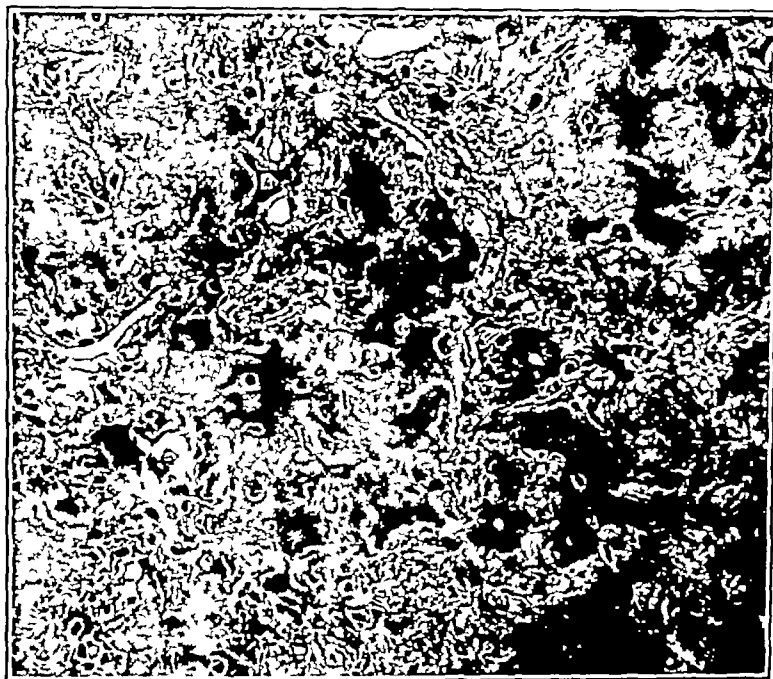


FIGURE 2 Photomicrograph of the Lesion of the Humerus
Note the trabeculae of calcifying osteoid tissue embedded in a cellular and vascular connective tissue, as well as the osteoblastic activity and the few osteoclasts

Our diagnosis was osteoid osteoma The culture showed no growth

DR ARTHUR L WATKINS Do these recur, Dr Larson?

DR LARSON As a rule, they do not In 1935, Jaffe¹ first described this lesion by reporting a series of cases, in 1940, he and Lichtenstein² published a follow-up and noted no recurrences in any of them

There is one important point about examining these people radiographically I think that I can demonstrate this by showing some slides This is a routine x-ray picture, in which you do not see the nidus If you suspect that a nidus is present, it is

is so that it can be removed surgically This is the same lesion after removal, and you can see the nidus in the gross specimen The bone you have to go through, as Dr Williams has pointed out, is extremely sclerotic

DR SNIFFEN These lesions, although first consisting of trabeculae of osteoid tissue, gradually calcify and thus become more radio-opaque

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- 1 Jaffe H L. "Osteoid-osteoma" benign osteoblastic tumor composed of osteoid and atypical bone *Arch Surg* 31 709 728 1935
- 2 Jaffe H L and Lichtenstein L Osteoid-osteoma further experience with this benign tumor of bone *J Bone & Joint Surg* 22 645-682, 1940

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That the home-guard physician has a clear-cut responsibility in the matter is suggested by the experience of a respected and capable pediatrician, returning after four years of military service, during which he was officially recognized for his devotion to duty, a colleague (or competitor) who had cared for some part of his practice in his absence was reported to have warned a patient, more or less directly, that three years in a fox hole had in no way contributed to her former doctor's capacity to re-enter the practice of pediatrics.

A people whose freedom has been preserved by a considerable effort on the part of several million of their countrymen certainly cannot be taken for bondsmen. They can be thought of only as free agents in their choice of physicians, regardless of any legislative rumbling to the contrary; they are not marked or branded; they are part of any practitioner's following only so long as he has the skill or personality to hold them. Any stay-at-home doctor who has benefited by the absence of another is in duty bound, however, to suggest to his colleague's patients not only that they are free to return to their former fold but that the decent thing would be for them to go there. Beyond that he is free unless he had entered into an agreement with his colleague to care for these patients for the duration only.

There must, as a matter of fact, be comparatively few of the remaining civilian doctors of merit who are interested in carrying their excess baggage any longer than is necessary. A considerable percentage of the survivors being fifty or more years of age, they may well be weary of too constant a struggle against bifocalism, of wrestling with the problems of nonavailable hospital rooms and absent nurses and of constantly dredging in the muddied channels of their memories for names that refuse to affix themselves to faces. They also know the weariness of war, even in its home-front aspects.

EPIDEMIC DIARRHEA OF THE NEWBORN

THE July issue of the *Quarterly Bulletin* of the Department of Health, City of New York, called attention to the increased number of outbreaks of epidemic diarrhea of the newborn that were re-

BACK TO THE OLD JOB

THE private practice of some 40,000 physicians who joined their country's forces during the past four years has, in a sense, been held in trust for them by those who stayed at home. These physicians have as much right to return to their old jobs, so far as such a thing is possible, as have the GI's whose jobs have been guaranteed them by force of public opinion. The difference is that the practitioner's job has been created by himself, over a period of years, and can be guaranteed to him only by the loyalty of his patients and the good faith of his colleagues who have been carrying on for him in his absence.

Dr Sidney Levin announces the opening of an office at 475 Commonwealth Avenue, Boston

Dr William Curry Moloney announces the opening of an office at 39 Bay State Road, Boston

SUFFOLK DISTRICT MEDICAL SOCIETY

The fall dinner of the Suffolk District Medical Society will be held at the Harvard Club of Boston on Saturday, November 17. Guests will assemble at 6 00 p m, and dinner will be served promptly at 7 00 p m. The speaker will be Brigadier General Elliott C. Cutler, M. C., A. U. S., whose subject will be "Experiences in the European Theater of Operations."

This is to be a "home-coming meeting," and all members of the district society are urged to bring as their guests men who have been recently discharged from service or those who are still in uniform, the latter will be admitted without charge, regardless of whether or not they are members of the Massachusetts Medical Society. In addition, the members of other district societies are urged to attend. Tickets may be purchased from the treasurer, Dr Richard S. Eustis, 319 Longwood Avenue, Boston 15. Contrary to the custom adopted for the past several years, wives of members will not be admitted.

MASSACHUSETTS SOCIETY OF EXAMINING PHYSICIANS

The fall meeting and dinner of the Massachusetts Society of Examining Physicians will be held on Wednesday, November 7, at 7 p m in the State Suite of the Copley Plaza Hotel, Boston. Dr Eugene E. O'Neil will present a paper, "Painful Extremities: The cause and treatment." Drs Burton E. Hamilton, William E. Browne, Alexander P. Aitken and Henry C. Marble will discuss the paper.

Reservations for the dinner (\$3.50 per person) may be made by writing to Miss Anne Rodman, Assistant Secretary, 157 Fourth Street, Medford, Massachusetts.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, November 1, at 7 15 p m in the classroom of the Nurses' Residence. Dr Eugene E. O'Neil will speak on the subject "The Diagnosis and Treatment of Venous Thrombosis." Dr Mary D. Matarazzo will be chairman.

LEGISLATIVE CONFERENCE

A meeting to discuss bills relating to health matters will be held on Thursday, December 13, at 10 a m, at the Gardner Auditorium, State House, under the joint auspices of the Massachusetts Department of Public Health and the Massachusetts Central Health Council. If necessary, the meeting will reconvene at 2 p m. Physicians, nurses and social workers interested in health promotion are invited to attend.

SALMON LECTURES

The current set of Thomas William Salmon Lectures will be given by Dr Roy Graham Hoskins on three successive Fridays, November 2, 9 and 16, at 8 30 p m at the New York Academy of Medicine. The subjects of the three lectures are as follows: "Biology of Man in Relation to Schizophrenia," "The Pattern of Schizophrenia," and "The Biological Appraisal of Schizophrenia."

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next written examination and review of case histories (Part I) for all candidates will be held in various cities of the United States and Canada on Saturday, February 2, 1946 at 2 00 p m. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination held later in the year. All applications must be in the office of the secretary by November 1, 1945.

All candidates are now required to be out of medical school eight years, and in that time they must have completed an approved one-year internship and at least three years of approved special formal training, or its equivalent by the preceptorship method under a recognized obstetrician, gynecologist or a diplomate of this board, in the seven years following the intern year. This board's requirements for internships and special training are similar to those of the American Medical Association, since both these organizations are at present co-operating in a survey of acceptable institutions.

A number of changes in regulations and requirements were put into effect at the Board's last annual meeting, held in June, 1945. These were designed to aid civilian candidates as well as those in the armed forces, they have been incorporated in the *Bulletin* of the Board, a copy of which may be obtained from the Secretary's Office, 1015 Highland Building, Pittsburgh 6.

All candidates are required to take the Part I examination, which consists of a written examination and the submission of twenty-five case-history abstracts, and the Part II examination, which consists of an oral, clinical and pathological examination. The Part I examination will be arranged so that the candidate may take it at or hear his place of residence, whereas the Part II examination will be held late in May, 1946, or early June, 1946, in that city nearest to the largest group of candidates. The time and place of the latter will be subsequently announced.

For further information and application blanks, address Dr Paul Titus, Secretary, 1015 Highland Building, Pittsburgh 6.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, NOVEMBER 1

FRIDAY, NOVEMBER 2	
*9 00-10 00 a m	Medical clinic Isolation Amphitheater Children's Hospital
10 50 a m	Postgraduate clinic in dermatology and syphilology Amphitheater Dowling Building Boston City Hospital
SATURDAY, NOVEMBER 3	
*10 00 a m-12 00 m	Medical staff round Peter Bent Brigham Hospital
MONDAY, NOVEMBER 5	
*12 00 m-1 00 p m	Clinicopathological conference Peter Bent Brigham Hospital
TUESDAY, NOVEMBER 6	
*9 00-10 00 a m	Medical clinic Infants Hospital
*12 15-1 15 p m	Clinicorontogenological conference Peter Bent Brigham Hospital
WEDNESDAY, NOVEMBER 7	
*12 00 m	Clinicopathological conference Children's Hospital
*12 00 m-1 00 p m	Clinicopathological conference Cambridge Hospital

*Open to the medical profession

OCTOBER 1-DECEMBER 10, 1945 and JANUARY 7-APRIL 22, 1946. Metropolitan State Hospital. Eleventh postgraduate seminar in neurology and psychiatry. Page 314, issue of September 6.

NOVEMBER 1. New England Hospital for Women and Children. Notice elsewhere on this page.

NOVEMBER 2, 9 and 16. Salmon Lectures. Notice elsewhere on this page.

NOVEMBER 7. Massachusetts Society of Examining Physicians. Notice elsewhere on this page.

NOVEMBER 8. Pitfalls and Pleasures in the Treatment of Diabetes. Dr. Elliott P. Joslin. Pentucket Association of Physicians. 8 30 p m. Haverhill.

NOVEMBER 17. Suffolk District Medical Society. Notice elsewhere on this page.

DECEMBER 13. Legislative Conference. Notice elsewhere on this page.

FEBRUARY 2. American Board of Obstetrics and Gynecology. Notice elsewhere on this page.

DISTRICT MEDICAL SOCIETIES

SUFFOLK

NOVEMBER 17. Harvard Club of Boston.

WORCESTER

NOVEMBER 12. Grafton State Hospital.

DECEMBER 12. Worcester City Hospital.

JANUARY 9. St. Vincent Hospital.

FEBRUARY 13. Worcester State Hospital.

MARCH 13. Worcester Memorial Hospital.

APRIL 10. Hahnemann Hospital.

MAY 8. Annual meeting.

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Number 18

SOME UNUSUAL ASPECTS OF CANCER OF THE BREAST*

ERNEST M. DALAND, M.D.†

BOSTON

CANCER of the breast in its early stages usually gives few if any symptoms, and ordinarily it is quite by accident that the patient notices a lump. If she waits until pain is a factor before consulting a physician, the disease is usually advanced. Unfortunately, she does not always seek medical advice at once and there is often a delay of several months.

The extent of the disease at the time of examination and treatment really determines the outcome in each case. It is known that there are varying degrees of malignancy, and that some cancers grow and metastasize more rapidly than do others. It is also known that there is a variation of growth at different ages, that cancer of the breast is less virulent in elderly than in younger women, and that there is a larger percentage of rapidly growing cancers in patients under forty-five than in those above that age group.

EARLY DIAGNOSIS AND TREATMENT

It is essential that the patient be taught to consult her physician if she notices anything wrong with her breast, whether it is deformity, inversion of the nipple, puckering of the skin or a lump. It is equally essential that physicians and surgeons be taught to act promptly when the patient does seek advice. It is better to explore many benign conditions than to let one cancer go untreated. The earlier the lesion, the more difficult is the decision concerning the exact nature of the condition. Truly early diagnosis and treatment was carried out in the following cases:

CASE 1 Ten years ago I was called by a physician's wife, who stated that she had just noticed a lump in her breast. Because of several cancers of the breast in her ancestors, she had made it a point to examine herself from time to time for possible cancer. She felt sure that the lump had not been there a week before. I examined her within an hour and found a tiny tumor with no characteristic signs of cancer.

*From the Pondville Hospital (Massachusetts Department of Public Health) Wrentham, Massachusetts and the Tumor Clinic of the Massachusetts General Hospital, Boston.
†Read by title at the annual meeting of the New England Surgical Society, Boston, September 20, 1944.

†Instructor in surgery, Harvard Medical School; chief of staff, Pondville Hospital; visiting surgeon, Massachusetts General Hospital.

At her insistence, she was taken directly to a hospital and the tumor was explored four hours after she first noticed it. It turned out to be a very small cancer without axillary involvement. A radical operation was done, and the patient has remained well.

CASE 2 A few months ago a patient consulted me with a complaint of itching in the breast for five days. She was unmarried and had never had previous trouble with her breast. Both breasts were large, but no tumor or other abnormality could be made out. Low down in the axilla, however, a hard lymph node measuring 2 by 2 cm. was palpated and it felt like cancer. A week later this node was explored and found to be malignant. A radical mastectomy was done at once. Even then nothing could be felt in the breast, but section of it showed a small cancer. This was, indeed, a peculiar early symptom: itching. During the week before operation the itching changed to deep aching in the breast.

CASE 3 A patient who consulted her physician for another ailment called his attention to a small puckering of the skin of the breast. No mass could be felt. Transillumination showed a disk of opaque tissue deep in the breast, extensive enough to make one suspect cancer. Operation was done three weeks later, and cancer, with involvement of several nodes was found.

AGE OF THE PATIENT

Cancer of the breast was formerly thought of as a disease of middle age, but as a matter of fact it may occur at any age after puberty. As previously mentioned, when it occurs in young people it is likely to be a rapidly growing cancer. Many of these patients, however, can be operated on successfully. In the following 3 cases, the patients were under nineteen years of age when operated on.

CASE 4 B. B. (P. H. 15183), a 15-year-old girl, was admitted to the hospital on February 8, 1939. She stated that 2 months previously she had been kicked in the left breast. Two weeks later she noticed a mass in the breast and consulted her physician. This was at the time of her first menstrual period.

Examination showed a hard mass measuring 2 by 2 cm. in the center of the left breast beneath the upper border of the areola and adherent to the skin. The areola was redder over this area than elsewhere. There was no lymph-node enlargement. X-ray films of the chest, spine, pelvis and femurs were negative for metastases.

Operation was carried out, and the tumor was removed. Frozen sections were interpreted as showing adenofibroma, but from the paraffin sections a diagnosis of adenocarcinoma was made. Three days later a radical mastectomy was done and more cancer was found. Of twenty-two lymph nodes examined, all were negative for cancer.

Twenty-two months later a mass measuring 5 by 5 cm. was felt in the posterior axilla. This was removed and found

to be a low-grade neurofibrosarcoma lying between the teres and subscapular muscles

-At the last examination, in April, 1944, there had been no recurrence of the tumors

CASE 5 V B (P H 22514), an 18-year-old, unmarried girl, was admitted to the clinic on June 15, 1944. One week previously she had noticed a lump in the right breast. A freely movable mass measuring 3 by 4 cm without adherence to the skin was noted in the upper portion of the right breast. It was thought to be an adenofibroma, but operation was advised and was performed on July 19. The tumor was slightly larger at that time, but no axillary nodes were palpable. Gross examination of the tumor and microscopic examination of a frozen section showed carcinoma. The wound was closed and a radical mastectomy was performed, with removal of the entire breast, both pectoral muscles and the contents of the axilla. The patient made a good operative recovery and was discharged 13 days later. The final microscopic report showed carcinoma simplex with foci of adenocarcinoma. There was also invasion of blood vessels by carcinoma. Twelve lymph nodes were identified, three of which showed invasion.

Nine weeks later the patient returned with a recurrent node in the right axilla and another above the right clavicle, pain in the lumbar spine and extensive involvement of the liver. She died on December 3 with extensive carcinomatosis, 6 months after the tumor was noted.

CASE 6 M S, a 46-year-old, unmarried woman was seen in consultation on January 13, 1945, for pain in the left breast. The right breast had been amputated at the age of 17 at the Homeopathic Hospital, Boston. Examination showed a scar of amputation, but the pectoral muscles were present. There was no evidence of recurrence, and the left breast was normal. Checking of the record at the Massachusetts Memorial Hospitals confirmed the amputation and revealed "clearing" of the axilla. The pathological report was cancer, and the axillary nodes were involved. From the examination it was apparent that the upper axilla had not been dissected, nevertheless, the patient was free from recurrence 29 years after operation.

UNTREATED CANCER

Several years ago, I¹ assembled the records of 100 patients with cancer of the breast who had died without any treatment except nursing care. The duration of life calculated from the onset of symptoms ranged from three months to thirteen years, with a mean duration of three years and four months. This study supplied a base line for use in determining the results of operative treatment. Our studies, fortunately, show a much greater life expectancy when operation is done than when it is not.

THE RADICAL OPERATION

In 1894, Meyer² and Halsted³ simultaneously described a radical operation that differed but little from the one now advocated. This consisted of removal of the entire breast with the overlying skin and the muscles and fascia beneath, as well as the contents of the axilla. Halsted advocated preservation of the clavicular portion of the pectoralis major. He also spared the pectoralis minor but divided it, dissected beneath it and resutured it. Meyer emphasized the importance of complete removal of all involved muscle in any cancer operation and hence recommended that both pectoralis muscles be removed. He also insisted that the lymphatic vessels between the two muscles should not be disturbed but should be removed *en bloc*. In 1918, Meyer⁴ again appealed to surgeons to carry out

this procedure, stated that he had not found it to be a mutilating procedure and that there was little loss of function of the arm.

In 1904, Warren⁵ wrote

It should always be remembered that the indications are in cancer to stamp out the disease. All other considerations which enter into so many other operations should be disregarded, with the single exception of the safety of life. Anatomy and aesthetics should always play a secondary role. It should be said here, however, that the modern operation, as now performed by the most conscientious surgeons, is always to be preferred to the feeble imitations that one often sees, even at the present time, in hospital practice.

In 1907, Greenough, Simmons and Barney⁶ stated:

The advantage obtained by removal of the pectoralis minor appears to consist in the greater ease with which the upper axilla can be dissected. It is not apparent that this muscle is especially liable to infiltration.

Cheattle⁷ and later Wainwright⁸ studied full sections of the breast, muscles and axilla. They demonstrated that both pectoral muscles become infiltrated with cancer and that the entire minor muscle must be removed. Wainwright⁹ further demonstrated the presence of lymph nodes on the anterior surface of the pectoralis major muscle. He emphasized the need of dividing the insertion of this muscle and of removing it without dissecting the fat from the anterior surface. He also pointed out the need of carefully removing the tissues on the anterolateral border of the latissimus. Handley¹⁰ demonstrated the necessity of removing the deep fascia and the rectus fascia because of the presence of lymphatic vessels in the fascia. He did not advocate the removal of much normal skin, but removed all the subcutaneous fat.

From all these sources has been evolved the technic of a radical operation that is generally accepted. This includes removal of the entire breast and overlying skin, all the pectoralis minor, all the sternal portion of the pectoralis major, the deep fascia down to the recti muscles and the entire axillary contents, with the exception of two nerves and one artery.

Patients to be submitted to radical operation must be carefully selected. Such operations should be carried out only if the disease is limited to one breast and the adjacent axilla. The axillary nodes must be movable if they are to be removable. The presence of disease above the clavicle, in the other breast or axilla, in the lungs or liver or in the bones is a contraindication to operation. Appropriate x-ray studies should be made to determine these facts. The age and general condition of the patient are obvious factors to be considered.

The prognosis in cases submitted to operation varies sharply according to whether or not the axillary nodes are involved. In the large clinics a five-year curability of 25 per cent is usual when the axillary nodes are involved, if they are not, the rate rises to 65 to 70 per cent.

EXCEPTIONS TO RADICAL OPERATION

There must be a good reason for substituting a simple amputation for the radical attempt at cure. Greenough¹¹ compiled figures from nine hospitals showing that simple amputations carried a curability of only 10 per cent, compared with 34 per cent for the radical operation.

The method advocated by Grace¹² of doing simple amputations and trusting to radiation to care for the metastatic nodes has little to recommend it. If the nodes are really cancerous, few cases are cured in this way. Grace reported 80 cases treated by simple mastectomy and x-ray, but stated that nodes that were large and easily accessible were removed, so that this did not actually comprise a simple mastectomy as it usually is defined. Forty cases were untraced. Grace claims 44 per cent cures for five years, based on the 40 cases that were followed. If all the untraced cases succumbed to cancer, the curability rate was only 22 per cent. He does not state whether this was a selected series in which only the minor operation was performed, nor does he give the ages of the patients.

However strongly one believes in the radical operation as necessary to cure cancer of the breast, it should be realized that there are times when a simple amputation is much wiser. This is done as a palliative measure, but occasionally one is fortunate enough to accomplish a cure. Simple amputation, however, is not so good as x-ray treatment in an inoperable cancer of the breast, particularly when there is involvement of the axillary nodes. X-ray treatment heals many ulcerated lesions and often prevents large cancers from breaking down. It retards the growth of the cancer and makes life more bearable, even though it may not greatly prolong life.

It has been our experience that many elderly patients do not tolerate massive x-ray therapy to the breast and, incidentally, to the lungs. We have seen several deaths follow such a course of treatment. As a result, when one is faced with the problem of treating a cancer of the breast in the aged, one must carefully weigh the possibility of performing a radical operation, even if it is done under novocain. If this is not feasible, simple amputation may be considered. Radium treatment has its place in a few cases.

In the following cases we believe that simple amputation was justified.

CASE 7 E. E., a 75-year-old, married woman was examined in February, 1944. She had a mass measuring 4 by 4 cm in the left breast, with no palpable nodes. There was hypertension, tachycardia and myocardial disease. It was believed that x-ray treatment would be unwise in a patient of this age because of the likelihood of pulmonary congestion and later fibrosis. After careful preparation by a cardiologist, a simple amputation was done under ether in 30 minutes. The patient was out of bed the day after operation and made a good recovery. Ten months after operation she was quite well, with no sign of cancer.

CASE 8 E. R., an 81-year-old, married woman was first seen in January, 1943. Shortly before examination she had noted a mass in the axilla. This was freely movable and measured 4 cm in diameter. Six years previously she had suffered a right hemiplegia. Four years previously a surgeon had done a right simple mastectomy for cancer. In February, an axillary dissection was done under novocain. The pectoral muscles and a segment of the axillary vein were removed. The patient sat up in a chair the following day and made a good recovery. She died on April 18, 1944, with no further recurrence.

CASE 9 E. D., an 82-year-old, unmarried woman, was seen in consultation because of a tumor of the breast of 6 months' duration. Both breasts were small, but in the left breast there was a mass measuring 4 by 4 cm, with adherence to the skin. There were no palpable nodes, and x-ray examination of the chest was negative. The patient was in fair physical condition, but was forgetful and showed signs of senility. She was extremely thin and would not have tolerated radiation treatment well. Under novocain, a quick simple amputation was done. Carcinoma was found. The patient left the hospital within a few days. She was well and apparently free from recurrence 2 years later.

CASE 10 C. G., a 49-year-old, unmarried woman, was examined on August 5, 1943. She had had a tumor of the breast for 5 years, but had done nothing about it until it broke down 3 weeks previously. Examination showed a foul, ulcerated carcinoma involving the entire central part of the breast. There were no palpable lymph nodes. X-ray films of the chest, spine and pelvis were negative for metastases. It was obvious that there was too much sepsis to consider a radical operation with exposure of the axilla. A simple amputation was done, with a pathological report of Grade 3 carcinoma. The patient made a good recovery and remained well until April 21, 1944, when a lymph node was found high in the axilla. An axillary dissection was done, and Grade 3 carcinoma was found in one node. The patient was apparently well 6 months later.

CASE 11 C. B. (P. H. 1153), a 51-year-old, married woman, was admitted on February 15, 1929. She had an extensive carcinoma involving the entire left breast. The tumor had been present for 2 years, but she had received no medical attention until 2 weeks previous to admission, when she had a hemorrhage. The entire mass, which extended from the infraclavicular region to the 9th rib and from the midline to the midaxilla, was ulcerated and foul. The first decision was to attempt to clean it up and to treat it by x-ray, but the odor was so bad that it was impossible for the nurses to dress it. The patient was anemic and presented a picture of prolonged sepsis. On February 25, the breast was removed by electrosurgery. The lower axillary nodes that were obviously involved were removed, but no attempt was made to remove the muscles or all the axillary nodes. The pathologist reported carcinoma simplex (Grade 3), with axillary metastases. The wound was left open. The patient received a course of deep x-ray therapy.

In September, she returned with a recurrent nodule 3 by 3 cm in the scar. This was excised. She was followed regularly until July, 1943, when she was readmitted at the request of her physician with dyspnea, cyanosis and considerable fluid in the chest. The case was diagnosed as cardiac decompensation and was treated by digitalization, with good effect. She was able to leave the hospital, but died of heart disease in January, 1944, 15 years after the first admission.

Comment: This palliative operation was done without expectation of cure, in the hope of relieving sepsis and making life more bearable for the patient. The operation was not the radical one usually thought necessary to cure cancer, but it was adequate for this slow-growing cancer.

CASE 12 A. J. W. (P. H. 3777), an 86-year-old, married woman, was admitted on September 26, 1931, with carcinoma of the left breast of a few months' duration. Because of her advanced age, operation was thought inadvisable and x-ray treatment was given. Two series of such treatments kept the lesion in check for nearly 3 years. It then broke down and began to discharge foul material. On July 19, 1933, the local tumor was excised under novocain. No attempt to remove the entire breast was made. Eight months later axillary metastases appeared, and 4 months after this several

nodules were found in the operative scar. The patient received additional x-ray treatments on four occasions, with good regression of the disease for a time, but died in February, 1937, from cancer and arteriosclerosis.

Comment It is probable that this patient should have had a simple amputation at the time of the first admission.

CASE 13 E G (P H 641) an 83-year-old, married woman, was admitted on June 15, 1928. A carcinoma of the breast had appeared 1½ years previously, and she had received a few x-ray treatments at another hospital. Examination showed a well preserved woman with a mass 6 cm in diameter in the upper outer quadrant of the left breast. There were no palpable axillary or supraclavicular nodes. Because of her advanced age a simple mastectomy was done under novocain anesthesia. The pathological report was carcinoma simplex. The patient spent the remainder of her life in various hospitals and nursing homes and died of cardiorenal disease at the age of 96. There never was any definite recurrence.

Radium was used in the following two cases

CASE 14 E C, a 78-year-old widow, was examined on June 7, 1941. She had a mass measuring 4 by 3 cm in the lower inner quadrant of the left breast. She was fairly well preserved, but the blood pressure was 250/118. Radical operation was not deemed possible. On June 13, the mass was excised under novocain and found to be a slowly growing adenocarcinoma. Fifteen radium needles of 3 mg each with a wall thickness of 0.5 mm of platinum were inserted in the breast so as to encircle the primary wound, which was closed. The needles were left in for 7 days for a total dosage of 7560 mg hr. The patient was last seen in November, 1944, with a questionable recurrence in the breast beneath the scar. She had never developed any involved lymph nodes.

CASE 15 C C, a 77-year-old, unmarried woman, was first seen in March, 1942, with a tumor of the left breast of 1 year's duration. There was a mass in the upper outer quadrant 2.5 cm in diameter, with a small, hard axillary node on the same side. The patient's physical condition was extremely poor. She had hypertensive heart disease and a large diaphragmatic hernia. Her physician would not permit a general anesthetic. Under novocain, radium needles were inserted into the tumor, which was found to be carcinoma, and into the axilla, according to the Keynes technic. These needles had a wall thickness of 0.5 mm of platinum and each contained 2 or 3 mg of radium. They were left in place for 7 days, for a total dosage of 8200 mg hr. Two months later 3000 r of high-voltage x-ray was given to one portal over the breast. An ulcerated area developed in the axilla and persisted several months. Under novocain the ulcerated area and a group of enlarged nodes low in the axilla were removed. No cancer was found in this material. Healing was slow. The patient remained free from disease nearly two years and died of diverticulitis of the sigmoid with abscess at the age of 80. Complete autopsy revealed no sign of cancer.

Comment In this case radium, x-ray and operation were used in turn. No one of the procedures as carried out was a major one, but the comfort that the patient received made her feel that they were worth while.

RECURRENT CANCER

It is rarely that surgery can be used in recurrent cancer of the breast. As a rule, radiation of recurrent nodules is better treatment when there is recurrence in the operative field. Involvement of the opposite breast or axilla in the absence of generalized disease calls for a decision whether further surgery is justified.

There have been 6 cases in which we have done a second radical operation. Two patients soon died of lung metastases, and 1 died seven years after the second operation. Of the other patients, 1 has been alive for ten years with recurrence, 1

has been well for five years, and 1 has been well for one year.

It has ordinarily been believed that if a patient lives for five years after operation for cancer of the breast and has no recurrence, her chances of cure are practically assured. It is true that most recurrences do appear before the end of five years, but it is not unusual to find them up to ten years. The following case shows a recurrence thirty-four years after operation, the latest that we have heard of.

CASE 16 G P (P H 20725), an 84-year-old, married woman, was admitted on September 10, 1942, with recurrent cancer of the breast. The referring physician, a well known surgeon, stated that he had performed a radical mastectomy for cancer in March, 1906. She had remained well until August, 1940, when a nodule appeared in the scar. Examination showed a scar of a Halsted incision, with absence of the pectoral muscles. In the lower axilla there was a nodular tumor measuring 7 by 5 cm, with ulceration and fixation to the chest wall. Throughout the scar and on either side of it there were numerous skin nodules. There were no enlarged nodes, but there was extensive pleural effusion. The patient died in December, 1942, without treatment.

The following cases demonstrate the comparatively low malignancy of certain breast carcinomas. Furthermore, they point out the necessity of dealing with various aspects of recurrence as they are found, keeping in mind that wherever there is life there is hope of palliation. Both these patients knew the nature of their disease, welcomed the possibilities of each new treatment suggested and co-operated to the utmost.

CASE 17 L U, a 41-year-old, married woman, had a simple breast amputation for cancer in 1913. A second operation for recurrence in the scar was done in 1918. In 1920, she was seen at the Huntington Hospital with an extensive carcinoma *en cuirasse* in and about the scar. She was given x-ray treatment. The disease was thus held in check for 7 years, but at the end of that time an ulceration developed. At the radiologist's request, we excised the ulcerated area and swung up a pedicle graft from the abdomen. Deep down in the excised area a few cancer cells were found.

We have followed this patient since 1927 and have carried out the following procedures: in 1928, coagulation of a recurrent skin nodule; in 1930, coagulation of recurrent skin nodules and wide excision of recurrences, with skin graft; in 1931, coagulation of nodules in the pectoralis major and ribs; in 1932, three operations for recurrence, with the use of pedicle grafts, dissection of the left axilla, with closure by flap from the arm, and partial resection of the sternum and three ribs, with rotation of the right breast to close the defect; in 1933, excision of a skin nodule; in 1934, a right radical mastectomy for positive axillary nodes; in 1935, excision of a recurrent nodule on the back; in 1936, resection of the stomach for gastric ulcer and removal of a gallstone; in 1938, excision of a recurrence on the arm; in 1939, the same; in 1940, excision of a recurrence on the chest wall; and in 1941, resection of the second rib. In 1942, a large supraclavicular node appeared. At first this responded well to x-ray treatment, but it has persisted and is now beyond further treatment.

Comment This patient is now 72 years old. She had the wrong operation at first, when she could have been cured. Since 1920, when her case appeared hopeless, she has had twelve major operations and ten minor ones. Between operations she has lived a useful life. She has been grateful for the relief given from each operation and has felt that life was wholly worth while.

CASE 18 E P (M G H), a 48-year-old, married woman, was seen in July, 1932, with carcinoma of the right breast, for which a radical mastectomy was done. A few months

*This patient died on July 20, 1945.

later she developed enlarged supraclavicular nodes on the same side and received x-ray treatment followed by complete disappearance of the nodes

In January, 1935, a lump developed in the right breast. This was thought to be cystic disease but it was explored. Carcinoma was found in association with cystic disease and a radical mastectomy was carried out.

In December, 1936, the patient entered the hospital complaining of vomiting for 2 weeks. A large mass was palpated in the right upper quadrant of the abdomen. X-ray examination showed complete obstruction of the second portion of the duodenum by an extrinsic mass. At operation metastatic breast carcinoma was found within the curve of the duodenum extending along the head of the pancreas involving the mesocolon and infiltrating the omentum. An anterior gastroenterostomy and an enteroenterostomy were done, with complete relief of symptoms.

After her recovery, the patient was told what had been found and what had been done. She then suggested x-ray treatment, on account of its success with the supraclavicular nodes, and the X-Ray Department agreed. She was given 2000 r to the anterior abdomen and 1800 r to the back, with the following factors: 200 kv, 0.5 mm copper and 1 mm aluminum filtration, through 15-by-15-cm fields at 50-cm distance, given at 200 r per day. The mass disappeared within 2 months and never reappeared. The patient had no more symptoms from this metastatic mass, although she lived for nearly 6 years after treatment.

From 1937 to 1941 pain developed in various parts of the spine, which was shown to be riddled with cancer. Small amounts of x-ray therapy were given, with prompt and complete relief for months at a time. In 1941, severe pain developed in the scapula. X-ray examination showed metastasis, and therapy gave no relief. Later a mass developed beneath the scapula, it was fluctuant and was thought to be an abscess. This proved to be a large lymph cyst pushing the scapula away from the chest. The patient drained large amounts of lymph from this time on. Later a mass of nodes appeared above the clavicle, and it was assumed that the thoracic duct was so involved that the lymph passed posteriorly beneath the scapula. There was no benefit from further radiation therapy.

The arm became badly swollen, but could be relieved as long as the lymph could be kept draining. A film of coagulated lymph tended to block the drainage area. Later, carcinoma developed in the sinus, and the patient died on September 10, 1942. There was no autopsy. No recurrences ever developed in the operated areas.

Comment. The chief features of this case, the history of which covered a period of 10 years, were bilateral mastectomies, complete relief of obstructing abdominal metastases by anterior gastroenterostomy, disappearance of the masses for five years as the result of x-ray therapy and the development of a lymph cyst from interference with the normal lymph channels by cancer.

SUMMARY AND CONCLUSIONS

Early diagnosis and treatment are essential for cure in breast cancer. Vague symptoms in the breast, deformity and lumps must be investigated.

Three cases of cancer of the breast in girls under nineteen are reported.

The ideal operation, if one is to attempt cure, is radical mastectomy, with removal of the entire breast, the pectoral muscles and the contents of the axilla. The steps in the gradual development of this operation are stated.

Exceptions may be made to performing the radical operation in certain cases if one is interested in palliation rather than in cure. Sepsis in the cancer, old age or poor physical condition may be sufficient reason for performing a simple mastectomy. Occasionally, but rarely, a five-year cure is obtained by this procedure. Several case reports of simple mastectomy and the reasons for it are submitted.

A case of recurrence thirty-four and a half years after radical mastectomy is reported.

Two cases of persistent recurrence of low-grade cancer over periods of twenty-four and ten years, respectively, are reported in detail.

483 Beacon Street

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BOSTON MEDICAL LIBRARY

Report of the President*

THE lapse of another year, the third of our participation in World War II, finds the Library carrying on its functions under the handicaps which embarrass the community as a whole, but hoping that when the war shall be won an orderly and successful plan for our continued development and growth may be put into effect. The formulation and activation of such a plan have engaged the constant consideration of your executive officers and trustees. More of this anon.

Our librarian, Dr. Viets, in his report, gives us an interesting discussion, which we have learned to expect, of the state of our collections, the accessions, the circulation and attendance, our relations with the *New England Journal of Medicine* and the *Journal of Bone and Joint Surgery* and other matters within his special domain. It is the duty of the president to speak of such issues as should be reported to the fellows of the Corporation, and which also ought to be of interest and concern to a wider medical public.

With regret, the deaths of eight fellows and of three nonresident fellows are recorded, as follows:

FELLOWS	ADMITTED TO FELLOWSHIP
Saul Berman	March 31, 1923
William B. Breed	July 14, 1922
William Pearce Coues	January 11, 1896
Sidney C. Graves	March 7, 1938
Richard Frothingham O'Neil	April 26, 1900
Edward Peirson Richardson	June 1, 1908
Charles Allen Riley	October 4, 1910
John J. Whoriskey	August 8, 1914
NONRESIDENT FELLOWS	
Mark H. Wentworth	November 7, 1917
Mortimer Warren	March 16, 1925
Emil Z. Ossen	February 19, 1936

None of these men could well be spared, but most had lived full lives and had made their appointed contributions to society. One, however, Dr. Graves, was ruthlessly cut down in his early prime, in the service of his country. I cannot forebear pointing to the loyal support of the Library on the part especially of three fellows who, although retired from active practice, continued their interest and financial help—Dr. Coues, Dr. O'Neil and Dr. Richardson, who had held fellowship for forty-eight, forty-four and thirty-six years respectively. We are led to believe that they thus found pleasure in meeting the obligation to support the interests of medicine in the broadest sense.

The regular monthly meetings of the Board of Trustees, held October to May inclusive, have been well attended, considering the exactions on time and strength caused by the war. The presence on the board of representatives of the administrations or

faculties of the three Class A medical schools in Boston assured a co-operative spirit in the approach to common problems. The members of the executive staff, headed by our indefatigable director, Mr. James F. Ballard, now in the fifty-third year of his service to the Library, have worked loyally and so efficiently that, shorthanded though they were, it is possible to say that the service has been maintained at a prompt and satisfactory level, although at the expense of a degree of strain and fatigue that cannot be maintained much longer without relief. The serious illness and final resignation during the year of Miss Lotta McCrea, so familiar a figure in Holmes Hall, is recorded with keen regret and an expression of sincere appreciation for her services as library assistant over a period of twenty-five years. Re-adjustments have been effected that made it possible to cover the work for the time being. Salaries have been raised in an attempt to offset the increased cost of living.

For details of our financial condition reference should be made to the report of the treasurer and of the independent auditors. Here it may be briefly stated that there was a slight decrease (\$225) in the dues received and also in the income from invested funds (\$589), these were more than offset by an increase of \$2478 from rents and maintenance, so that total income shows an increase of \$1738 over the year before. Unfortunately, however, the total expenses increased by \$4699, which resulted in a deficit for the year of \$3049. We received under the will of Mrs. Annie H. Farlow, widow of Dr. John F. Farlow, former librarian, a generous unrestricted bequest of \$10,000. This enabled us to discharge our bank loan of \$5000, incurred to enable us to pay for certain necessary alterations in our building last year. Grateful acknowledgment is made to the Suffolk District Medical Society, which voted to continue the payment of a generous sum annually, which in former years was normal compensation to the Library for services rendered, but which lately has been only in part earned, because the society has not made the same use of the Library's facilities.

A superficial consideration of these figures, which show but a small operating deficit at a time when the war has played havoc with most civilian enterprises, gives a very wrong impression of the organic health of the Library. To the uninitiated it may appear to be a thriving institution where one of the best collections of medical books and periodicals in the United States may be consulted amid convenient, comfortable and tasteful surroundings, aided by a competent and courteous staff. Actually the trustees and our friends who advise with them know that the statement in last year's report that "the Library is in danger of stagnation unless its

*Presented at the annual meeting of the Boston Medical Library, March 6, 1945.

resources can be materially increased" must be regarded as an understatement. The Library is stagnating, and the additional income and endowment then estimated as necessary should be more than doubled to enable us to meet our opportunities for service. This is not the place to describe in detail the plans that the trustees are trying to realize, but a general statement may be made about the one that seems to have the most to commend it—namely, the Library should continue to be developed as a central research library in the field of the medical sciences, assuming the burdens and responsibilities pertaining to that status and relieving the Class A medical schools, hospitals and laboratories of Greater Boston or, it is hoped, of a much larger area, of the necessity of each assembling more than a first-rate working library within its own walls. Thus the ever-recurring problem of finding more space for these growing accumulations would be solved by depositing less used or rarer volumes in the central library and borrowing from it the more unusual books and periodicals. In return for such service the institutions would make appropriate annual contributions to the operating income of the Library.

The trustees and their advisers hope that a quarter of a million dollars may be given by some far-sighted charitable or educational agency for the completion and rehabilitation of our physical plant, especially our stacks and periodical and reading rooms. They are convinced—and indeed have been advised—that such a sum of money cannot be obtained unless the Library can raise from its fellows, from physicians at large and from public-spirited citizens an equal sum, which, properly invested, would afford a substantial addition to our income. Additional income would be obtained from the institutional contributions above men-

tioned, from an increase in the number of our fellows and perhaps from higher yearly dues, which at the present level of \$15 may be compared with the \$40 dues of the New York Academy of Medicine and the \$30 dues of the College of Physicians of Philadelphia. In other words, the local community, especially the doctors, must give evidence that we deserve assistance in this project because we are determined to help ourselves. Undoubtedly a medical library makes little appeal to the average layman, whose generous emotions are easily stirred by campaigns for the control of certain diseases, such as cancer, tuberculosis and infantile paralysis, or for the promotion of some special therapeutic method, such as physical therapy, or for the support of hospitals or of various research problems. Nevertheless, it ought not to be difficult to convince any intelligent layman that the foundation and background of all these noble enterprises consist of the printed records of what has gone before, without which records accumulated, stored, classified and made easily available every new research and study would have to start from scratch!

The house and the collections of the Boston Medical Library are valued at one million dollars,—a conservative figure, for many of the files of periodicals, the historical items and the incunabula could scarcely be replaced at any price. Unlike the orchid, it cannot live on air and admiration, the founders rooted it sturdily in the soil, and on the soil it must continue to depend for its support. Let those who have enjoyed its privileges remember it in their wills, let it be commended to public-spirited citizens who both by gift and by bequest have shown their willingness to support the institutions that make our community so much to be envied.

DAVID CHEEVER, *President*

Report of the Librarian*

THE Library passed through its third full year of war without damage by bombs or serious curtailment of its normal functions. It is gratifying to note that during 1944 our membership actually increased from 873 to 903, in spite of the fact that of the total membership in all classes, 177, or nearly 20 per cent, were in service with the armed forces of the United States. Also, the circulation of books and the attendance both increased over the 1943 figures, thus indicating a healthy return toward the normal of prewar usefulness. Within a year or two the Library will contain 200,000 volumes and 135,000 pamphlets, in addition to collections of portraits, medals and other items of medical interest. Four hundred and sixty-six periodicals were re-

ceived in 1944, lacking, of course, almost all French, German and other foreign-language journals. We had intimations in 1945 from foreign correspondences that some journals published in Europe during the war were safely stored and would be sent to us at a later date. Of American journals, we have retained many extra copies for our European friends.

The Library, thus, has been reasonably well maintained, and in spite of many members' being away in service or otherwise engaged in war efforts, more use of it was made daily than in previous war years. This state of affairs is indeed gratifying to the librarian, who, unlike some of his fictitious or real predecessors, would not mind if all the bookshelves were empty and the books under his care were aiding scholarship and helping to advance medical knowledge.

*Read in part at the annual meeting of the Boston Medical Library March 6, 1945. Additional material will appear in the author's reprints and in the Sixty-Ninth Annual Report of the Boston Medical Library (Boston 1945).

BOOK-REVIEW DEPARTMENT

The Library has continued to review books for the *New England Journal of Medicine*. In 1944, it was only possible to review in an extended manner seventy-seven books but, in addition, as each book was received, a brief notation of its contents was published. As usual, the list of the reviewers appeared in the indices of the current volumes of the

the year 1943 and writes "[His publishing house] considers the book reviews in the *Journal* to be of unusually high quality, much above the average medical book review. There are far too few constructive criticisms of medical books, and the *Journal*, with its careful reviews, performs a real service not only to its readers but to its authors." The writer also expresses his thorough approval of

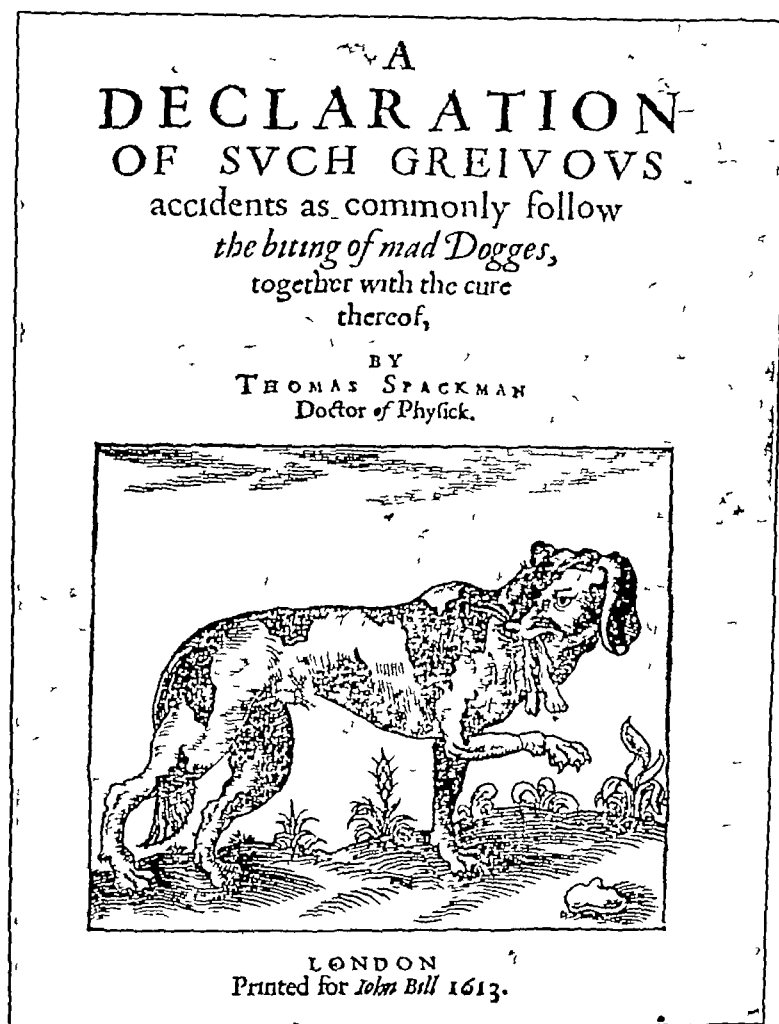


FIGURE 1 Title Page of *The Biting of Mad Dogges*

Journal. In the future, because on at least one occasion a competent reviewer was severely criticized by the author of a book, it seems best to the librarian to preserve the anonymity of reviewers even further so that disagreeable incidents, of no particular importance in themselves but nevertheless to be avoided, will not occur in the future. That the publishers of medical books appreciate the book-review service is emphasized by a letter from Mr. T. A. Phillips, of the J. B. Lippincott Company, printed in the August 10, 1944, issue of the *Journal*. Mr. Phillips comments on the librarian's report for

unsigned reviews. With this statement the librarian is fully in accord.

ACCESSIONS

With the special book funds available to the librarian, purchases were made in 1944 following out the well established lines of accession used by the Library in the past. Interest in incunabula has been continued, but few are now offered by booksellers that are not already on our bookshelves. We have expanded our collection of English imprints issued before 1640 and have continued to grow in

ther departments. A few books of particular interest are worthy of special notice

Incunabula

Only one incunabulum was acquired during the year. This, a German broadside, *Almanach auf das*



FIGURE 2 Title Page of Rosa Gallica

Jahr 1481, adds another *Aderlass* calendar to the fifteen broadside almanacs already in the Library. The following years are now represented 1470, 1472, 1476, 1477, 1478, 1481-2, 1484, 1485, 1487, 1492, 1494, 1496 and 1499. Most of the almanacs, either broadsides or broadsheets, are bleeding calendars, but some also indicate favorable times for purging. In addition, one manuscript and five incunabula volumes contain calendars or almanacs.

English Imprints Issued Before 1640

To our small but growing collection of books printed in England before 1640, thirteen volumes were added in 1944. Of particular interest is a copy of the first edition of *The Method of Physicke*, by Philip Barrough, issued in London in 1583. There are only two other known copies of this edition.

The book, on the causes and signs of disease, as well as the remedies used in treatment, was a popular sixteenth-century text and is known in eight or more editions. Barrough (or Barrow) studied medicine in Cambridge and later practiced in London.

Of great rarity is the first edition of *The Whole Course of Chirurgerie* by Peter Lowe, published in London in 1597. Lowe, an army surgeon of wide experience, had studied surgery in Paris. After a long career in France he returned to his native Glasgow, where he founded the Faculty of Physicians and Surgeons in 1599. His book *The Spanish Sicknes* (1596) was followed the next year by his *Chirurgerie*, the outcome of his experiences in France. Lowe

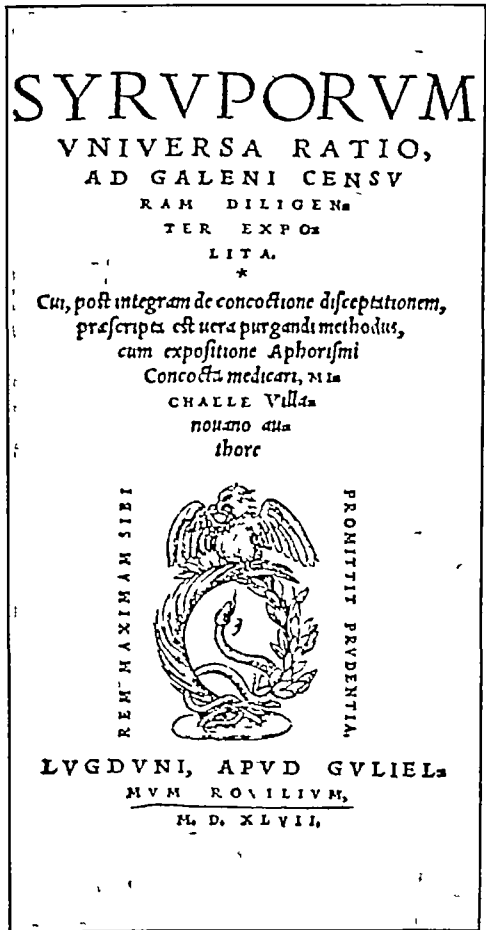


FIGURE 3 Title Page of Syruporum universa ratio

describes amputation of the leg, the reduction of hernia and the use of the truss. Particularly noteworthy are the clear illustrations. Finlayson wrote a fine biography of Lowe, and D'Arcy Power discussed the *Chirurgerie* in one of the 1927-1928 issues of the *British Journal of Surgery*.

A third volume is by an almost unknown doctor, Thomas Spackman. *A Declaration of Such Greivous*

Incidents as Commonly Follow the Biting of Mad Dogges together with the Cure Thereof was published in London in 1613. The literature of dog bites and hydrophobia was quite thoroughly reviewed by Spackman, who, in spite of thirty years of practice, saw few cases. He urges a more careful study of the

Sixteenth-Century Books

Among the books printed in the sixteenth century, other than the English imprints separately noticed, four have more than passing importance.

Two are books by, or attributed to, Symphonien Champier, an active personality and practitioner

**Antidotale preservatiōis: cum addi-
tionibus: in epidimicū morbum: ob
plurimorū vtriusq; serus cōmodita-
tem: ex canonibus medicinalibus.**

**A Martino Stainpels Viennēse
Artium & Medicinē doctore
salutifere elaboratū cernit.**

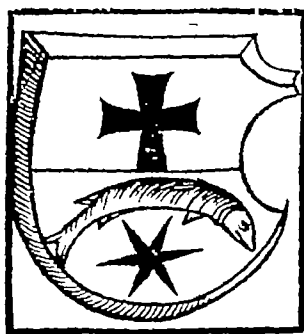


FIGURE 4 Title Page of *Antidotale Preservatiōis*

subject by physicians and suggests the use of scarification, cupping and cauterization of wounds. He describes in some detail the symptoms of hydrophobia. The book is dedicated to Sir Robert Wroth, a well known English sportsman of the time, and contains sound arguments for prevention. The title page gives a striking illustration of a rabid dog (Fig. 1)

of medicine in Lyons. *Rosa Gallica* (Fig. 2) was printed at Paris by Jodoens Badio, known as Ascensian, and is No. 90 in the check-list of the writings of Symphonien Champier by Ballard and Pijoan. The Library has also acquired another edition of *Practica Nova in Medicina*, published in Venice in 1522, this being the third printing of the book owned

by the Library In Ballard and Pigoan's check-list it is No 82

A third addition, *Syruporum uniuersa ratio* (Lyons, 1547) (Fig 3), written by the ill-fated Michael Seruetus, — or Villanovano, as he then thought best

library, particularly one not usually listed It was Champier, incidentally, who made a home for Seruetus in Lyons and caused him to study medicine The fourth book of note is *Antidotale preseruatoris*, by Martino Stainpeis (Fig 4), issued in

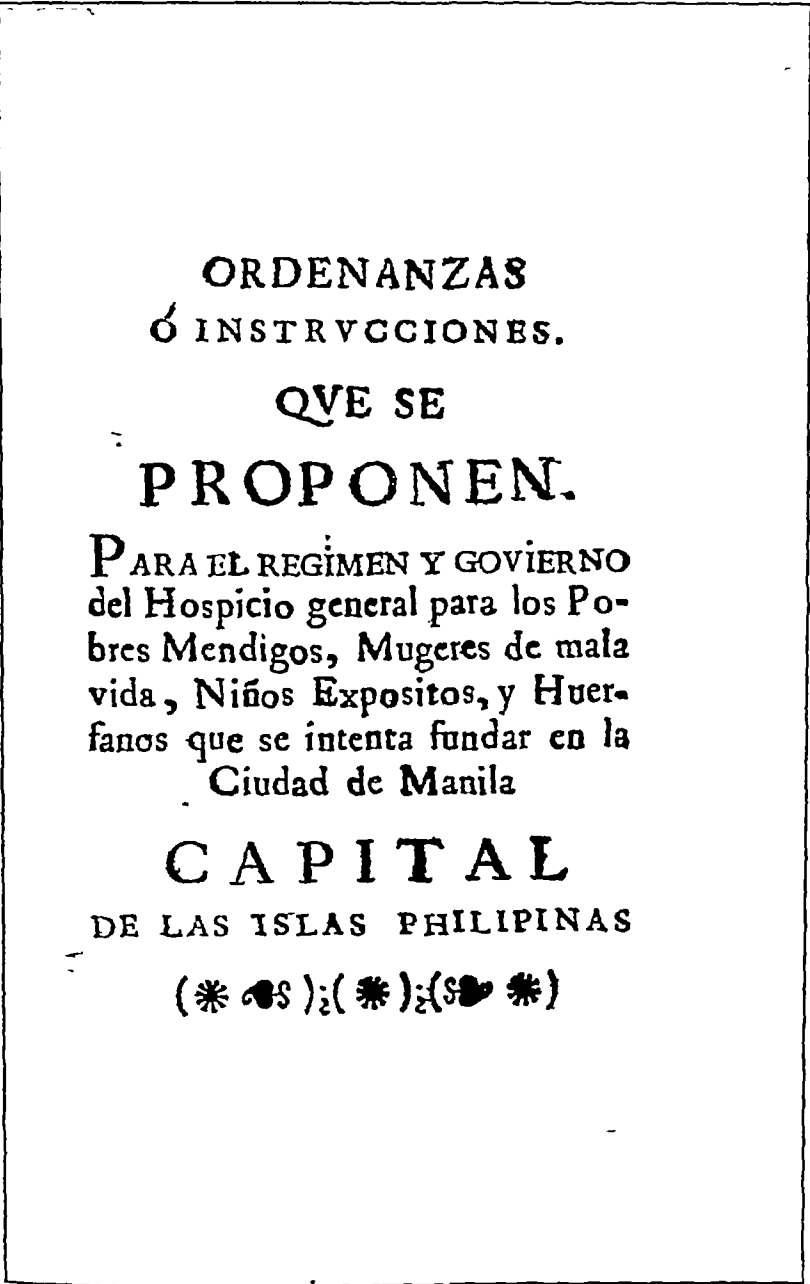


FIGURE 5 Title Page of the Ordenanzas 6 instrucciones Hospicio General Manila
Contained in Remedio Politico

to call himself, — is a criticism of Galen's general theory of syrups The book was originally published in Paris in 1537, and was popular enough to be reprinted at Venice in 1545, as well as in Lyons in 1546 and 1547 Since all issues of this book are scarce, any edition is a welcome addition to a medical

Vienna in 1510 It was printed by Johannes Singrenius This is an early sixteenth-century plague tract by a little known author
Varia
Of timely interest are the early Philippine imprints, particularly in view of the destruction by the

Japanese of the central scientific library of the Philippine Government in Manila. The library, one of the largest and most carefully selected accumulations of scientific books in Asia and Malaysia, was, according to the April 20, 1945, issue of *Science*, a remarkable assemblage of basic literature. The loss is an irreplaceable one.

The Library has acquired an account of the political and civil state of the Philippines in 1779, by Manuel del Castillo (Fig 5), containing the ordinances and rules of the Government General Hospital at Manila, when under Spanish rule. It was printed at Sampaloc, a district of Manila.

Occasionally there drops on the librarian's desk a heart-warming book, often a by-product of medicine. Such delightful creations temper the load of textbooks and monographs and not only illustrate how versatile are our fellow doctors, but also show their fundamental interest in "the spirit in which the gift is rich," be it of gold or myrrh. McNair Wilson's *British Medicine*² may indeed seem at first to be a slight contribution to medical history, yet this brief text re-emphasizes our great debt to British medicine in an informative and pleasing manner, with superb illustrations, many of them in color. Not a few of the portraits are relatively unfamiliar to American physicians, such as the striking Orpen painting of Sir Clifford Allbutt, Osler's "brother Regius" at Cambridge, now in the Fitzwilliam Museum.

Pleasing, too, is the reprint by the Merrymount Press, made at the instigation of Dr. Joseph H. Pratt, of Osler's well known paper of nearly four decades ago entitled *Vienna after Thirty-four Years*.³ It is in this paper that Osler recalls, as fellow students in 1874, Fred Shattuck, E. H. Bradford, E. G. Cutler and G. K. Sabine, of Boston. One only wishes that Pratt, who was with Osler at the time, had added his reminiscences to those of his distinguished teacher.

To these may be added the first printing of a travel diary by Harvey Cushing,⁴ issued under the editorship of Dr. John F. Fulton, who is preparing a biography of Dr. Cushing. As was his custom, Cushing kept a diary of a brief holiday trip, in 1900, to Le-Puy-en-Velay, in southern France. His pocket sketchbook contained not only the diary notes but sketches, some of them colored, of what he observed and thought worthy of recording. The drawings show great delicacy of line and color. The medical world welcomes this glimpse into a little known aspect of a great surgeon's life.

One other book, entirely different from those already mentioned, is worthy of a place here. Dr. A. J. Cronin's *The Green Years*⁵ gives a penetrating analysis of a boy's struggle during his formative years in a small Scottish town. The boy, born in Ireland, finds life none too easy as a Catholic in a hidebound Protestant community, intolerant to an almost unbelievable degree. There is little of medi-

cine in the story but much of rich human nature, as could only be observed and retold by a doctor.

Our collection of travel books by doctors was enriched by the addition of *Epitome trium terrarum partium, Asiae, Africae et Europae* (Zurich, 1533) by Joachim Vadianus, *Medicinisches-chirurgische Beobachtungen auf seinen Reisen durch England und Frankreich, besonders über die Spitäler* (Vienna, 1783) by Johann N. Hunczovsky and *Travels in the Morea, Albania, and Other Parts of the Ottoman Empire* (London, 1813) by F. C. Poqueville. Vadianus (1484-1551), born Joachim von Watt, in St. Gallen, Switzerland, became dean of the University of Vienna and later practiced in Zurich. Hunczovsky, a Czech, born in 1752, visited hospitals in England and France in 1776-1777 and wrote about the Hunters, Pott and Lind in England and David Fournier and others in France. He later became professor of medicine in Vienna. Poqueville, a French doctor, was held by the Turks in Greece for three years during the Napoleonic War. He was allowed to travel, and noted much of interest about the country and its people, medical customs and practice. At a time when travel books were widely read in England, the book was well translated from the French and published in a large quarto, similar to many works by English physicians of the time.

Certain books and journals of unusual interest have received editorial comment in the *New England Journal of Medicine*. Obendorf's *The Psychiatric Novels of Oliver Wendell Holmes*, Cushing's *A Bio Bibliography of Andreas Vesalius*, Wood's *The Art of Falconry*, *of Frederick II of Hohenstaufen* and the new *Journal of Neurosurgery*.

Art Anatomy

The Library has enlarged its collection of books on art anatomy, and nine volumes in this class were added in 1944. A useful accession was *Les quatre livres de la proportion des parties et pourtraits des corps humains*, by Albrecht Dürer, published in Arnheim in 1614. Dürer's famous book *Human Proportions*, first published at Nuremberg in 1528, was issued in many editions and languages in the sixteenth and seventeenth centuries. In addition to this late French translation the Library has copies of the first edition, in German (Nuremberg, 1528), the first Latin edition (Nuremberg, 1532), the first edition in French (Paris, 1557) and the first Italian edition (Venice, 1591).

Dürer's plates were frequently copied by almost every writer on the subject after 1528. No exception was Richard Haydocke, a young student at Oxford at the close of the sixteenth century. Traveling on the Continent as a young man, he became interested in art, anatomy and engraving. The work of Giovanni Paolo Lomazzo, a Milan painter, attracted his attention, and on returning home he translated Lomazzo's book into English. He dedicated the

work to Thomas Bodley and had it published in Oxford in 1598, under the title *A Tracte Containing the Artes of Curious Paintinge Carvinge and Buildinge, written First in Italian by Jo Paul Lomatus, Master of Milan, and Englished by R II, Student Physik*. In the book are the Dürer plates, but even greater interest is the engraved title page giving a portrait of Haydocke in his ruff and gown, as a "student of physik". At Oxford he was much influenced by John Case, the physician and writer on Aristotle. He received his medical degree in 1601 and later in life practiced in Salisbury.

Manuscripts

Reflecting the practice of medicine in this country about 1800 is a large series of letters to and from Dr Levi Bartlett, of Kingston, New Hampshire, written between 1787 and 1806. Of particular interest to Massachusetts are the records of meetings of the Suffolk Medical Society, including a list of members. The Society first met in Dedham on November 7, 1785, having been projected at a preliminary meeting in Walpole on September 5 of that year. The records acquired by the Library cover the period from the beginning through May 4, 1789. Membership was confined to physicians practicing in fifteen towns south of Boston. Dr Cotton Tufts, of Weymouth, also one of the most active of the group founding the Massachusetts Medical Society a few years earlier, was elected the first president.

During 1944 the following publications appeared under the authorship of officials of the library:

PUBLICATIONS

A Catalogue of the Medieval and Renaissance Manuscripts in the Boston Medical Library. Compiled by James F. Ballard. 246 pp. Boston privately printed, 1944.

Viets, H. R. Report of the librarian, Boston Medical Library. *New Eng J Med* 230 760-765, 1944.

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Sixty-eighth Annual Report of the Boston Medical Library. 32 pp. Boston privately printed, 1944.

Viets, H. R. *An Introduction to a Catalogue of the Medieval and Renaissance Manuscripts and Incunabula in the Boston Medical Library*. Reprinted and revised. 14 pp. Boston privately printed, 1944.

Viets, H. R. Medical education: old purposes and new methods. *Rhode Island M J* 27 511-514 and 553, 1944.

The Boston Medical Library Medical Classification Part One—Schedules. Compiled by James F. Ballard. Third edition, revised. 46 pp. Boston privately printed, 1944.

Ballard, J. F. Medical books of 1943. *Bull M Library A* 32 391-395, 1944.

* * *

The Library has continued to enjoy its cordial relations with the *New England Journal of Medicine* and the *Journal of Bone and Joint Surgery*, both occupying quarters in the Library building.

During the year, the director and the librarian were made honorary consultants of the Army Medical Library, Washington, D. C., and the librarian served on the Executive Committee. The librarian attended the fiftieth anniversary of the founding of the Cleveland Medical Library on November 27, 1944.

HE PY R VIETS, Librarian

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LIVER ABSCESS, PNEUMONIA AND EMPYEMA DUE TO FRIEDLÄNDER'S BACILLUS IN DIABETES MELLITUS*

A Report of Two Cases, with Recovery in One

E. PAUL SHERIDAN, M.D.†

BOSTON

FEW cases of liver abscess due to Friedländer's bacillus (*Bacterium friedländeri*, *Klebsiella pneumoniae*) are to be found in the medical literature. Boettiger et al.,¹ in a review of articles in English, German and French literature since the beginning of the century, found only 25 such cases; they reported 2 cases, with autopsy findings. Rothenberg and Linder² had 2 cases of solitary liver abscess due to Friedländer's bacillus, with recovery. Eliason³ describes a case of a solitary liver abscess due to the same organism, with recovery. The following 2 cases are reported as the only ones known among more than 20,000 diabetic patients treated at the George F. Baker Clinic.

CASE REPORTS

CASE 1. A. B. (No. 19163), a 65-year-old man, entered the hospital on April 8, 1940, complaining of marked weakness for 6 months and drowsiness for 3 days. Diabetes mellitus had been discovered in 1933, but the patient had refused insulin and dietary control in spite of continued loss of weight, polyuria and polydipsia.

On admission the temperature was normal, the pulse 108, the blood pressure 90/60, and the respirations 20. There was emphysema of both lungs, but there were no rales or areas of dullness. The liver edge was palpable 6 cm. below the right costal margin and was tender. The blood-sugar level was 120 mg. per 100 cc., and the urine contained 3 per cent sugar. Forty units of regular insulin was given 4 hours before admission, which probably accounted for the normal blood-sugar value. The white-cell count was 37,500, with 93 per cent neutrophils.

Twenty-four hours after admission the patient had a severe chill and the temperature rose to 102°F. X-ray examination of the chest revealed several areas in the left lung suggestive of an inflammatory process. The patient was seen by an ophthalmologist because of blurred vision, and a diagnosis of metastatic choroiditis was made. A blood culture was taken, and Friedländer's bacillus was identified 48 hours later. The spinal-fluid smear and culture were likewise positive for the organism. Intravenous sodium sulfapyridine and a whole-blood transfusion were given, with little or no improvement clinically. On the 8th day, however, the blood and spinal-fluid cultures were sterile. The following day anti-Friedländer-bacillus (Type A) serum (Lederle) was given, and the patient appeared to be improved. On the 17th day, incision and drainage of an abscess of the left lung were performed, and a culture from the abscess showed the Friedländer organism. There was no improvement, and the patient expired 21 days after admission.

Autopsy. Post-mortem examination revealed a single abscess of the left lung, which had been drained, and a small area of recent pneumonia. The right lung was clear. The liver contained multiple abscesses, and there was a single abscess in each kidney. Cultures from all the abscesses yielded Friedländer bacilli. The brain showed an encapsulated meningitis, but a culture from the cisternal fluid was sterile.

CASE 2. C. D. (No. 24933), a 56-year-old, Jewish man entered the hospital on April 22, 1944, complaining of chills, fever and loss of weight. Diabetes mellitus had been discovered in

1928, but the patient had never taken insulin or followed a diet. During the previous 4 months he had a "cold," and during the 2 weeks prior to admission he had experienced recurring chills, fever and pain in the lower right side of the chest.

On admission the temperature was 103°F (rectal), the pulse 100, the blood pressure 120/80, and the respirations 28. The important findings were limited expansion of the chest on the right side, dullness to percussion over the right lower lobe and rales heard over the middle lobe and in the axilla. The liver edge was felt three fingerbreadths below the margin, and there was tenderness in the right upper quadrant of the abdomen. The spleen was palpable 1 fingerbreadth below the costal margin. The red-cell count was 3,570, and the white-cell count 14,200, with 83 per cent neutrophils. A blood Hinton reaction was negative, and the blood sugar level was 312 mg. per 100 cc. The urine contained 3.8 per cent sugar. X-ray examination of the chest revealed obliteration of the right costovertebral angle. A flat plate of the abdomen was negative. Stool examinations were negative for amebae.

With the aid of repeated transfusions, careful control of the diabetes and a high-carbohydrate intake, the patient prepared for operation. During that time various liver function tests were performed. The bromsulfalein test re-

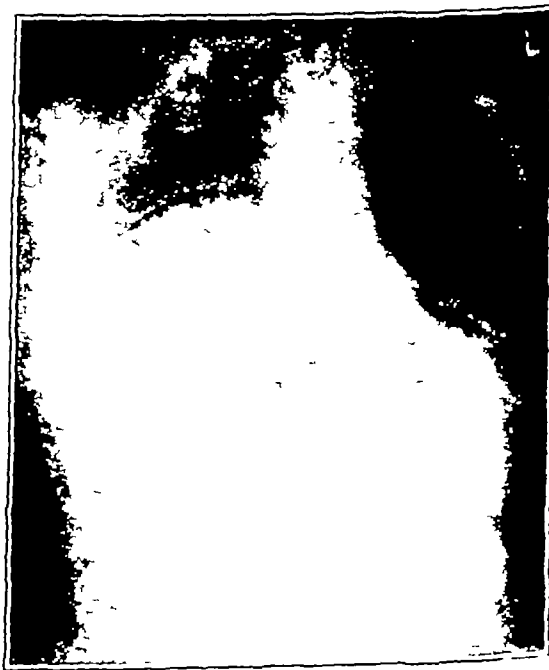


FIGURE 1. Roentgenogram taken on May 22, 1944.

vealed 53 per cent dye retention. The prothrombin time was 81 per cent. The serum protein was 6.1 gm. per 100 cc., with an albumin of 3.1 gm. and a globulin of 3.0 gm. X-ray examination of the upper gastrointestinal tract and intravenous pyelograms were essentially negative.

The patient continued to run an extremely septic type of temperature, with recurring chills, and the tenderness in the right upper quadrant of the abdomen became well localized. On the 24th day, an exploratory operation was per-

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formed and 5 cc. of purulent material was aspirated from a solitary liver abscess, in which a drain was placed. Bacteriologic examination of the fluid showed a gram-negative rod with a capsule, and on culture this proved to be a Friedländer's bacillus. The fluid removed from the right pleural cavity and the sputum likewise contained this organism. Six blood cultures were taken, and all were sterile. Penicillin, 100,000 units daily, was begun 4 hours after operation and



FIGURE 2. Roentgenogram taken on September 21, 1944

was continued for 7 days, with no apparent effect. Then, sulfadiazine, 6 gm. daily, was started, and within 60 hours there was marked improvement, as evidenced by a normal temperature and the patient's general appearance. During that time the chest findings had progressed so that there was involvement of both lungs. Figures 1 and 2 show the x-rays of the chest taken at various stages. During the course of his disease, the patient received nine transfusions of whole blood.

The patient began to gain weight, was allowed up, and was discharged 65 days after admission. He required 12 units of protamine-zinc insulin and was placed on a diet of 182 gm. of carbohydrate, 89 gm. of protein and 105 gm. of fat.

The debilitated condition of these patients as due in part to the fact that their diabetes had been uncontrolled for many years. Such patients should be susceptible to the Friedländer organism, and it is surprising that this type of pneumonia is not encountered more frequently than it is in diabetic patients. The latter fact again illustrates the highly specific character of the reaction between uncontrolled diabetes and bacterial infection. Thus, the diabetic patient has low resistance to the tubercle

bacillus and pyogenic organisms, especially *Staphylococcus aureus*, but no unusual incidence of pneumonia, meningitis or syphilis is encountered among these patients.

The history of cough and the pulmonary changes suggest the respiratory tract as the portal of entry. In both cases, however, the pulmonary manifestations became most pronounced after there had been extension to some other organ. In Case 1, the meningitis was succeeded by an increase in the pulmonary findings and a gradual progression to abscess formation, and in Case 2, both lungs became involved after the development of the liver abscess.

The above cases present the usual findings of liver abscess — chills, fever and an enlarged, tender liver. In the recovered case such symptoms were marked throughout the preoperative course. There were few chills after the operation, but the fever did not subside until after sulfadiazine was begun.

The management of diabetes in such cases is accomplished by adequate doses of protamine-zinc insulin and crystalline insulin to utilize a high-carbohydrate diet. On the days when the carbohydrate intake was less than 100 to 125 gm. by mouth, glucose was given intravenously and additional insulin was administered to ensure its utilization. The repeated use of whole-blood transfusions is advised, since marked reduction of the red-cell count occurs with this infection. The recovered patient received nine transfusions during his entire course. The use of sulfadiazine in such doses as will maintain a blood level of 8 to 11 mg. per 100 cc. is recommended. The response to this therapy was remarkable in the recovered case, and in Case 1 the administration of sulfapyridine resulted in sterile cultures of both the blood and the spinal fluid.

SUMMARY

Two cases of liver abscess due to Friedländer's bacillus bacteremia and occurring among 20,000 diabetic patients are reported.

The use of sulfadiazine, repeated blood transfusions, surgical drainage and control of the diabetes with insulin and diet are advised in the treatment of similar cases.

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MEDICAL PROGRESS

THE PATHOGENESIS OF RENAL INSUFFICIENCY (Concluded)*

STANLEY E. BRADLEY, M.D.†

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Acute Infections

Renal blood flow increases strikingly during fever induced by the administration of a foreign protein (the so-called "pyrogenic reaction"), apparently as the result of efferent arteriolar vasodilatation.⁷⁴ The systemic circuit is likewise profoundly affected.⁷⁵⁻⁷⁷ Peripheral vascular resistance decreases, whereas the cardiac output increases and maintains the blood pressure. This balance, however, may fail, probably as a result of a failure of cardiac output to compensate completely for the reduction of peripheral resistance, and circulatory collapse ensues. Studies of renal function have never been made in this phase of the pyrogenic reaction, and it is not known whether renal vasoconstriction follows vasodilatation. The hyperemic response is not mediated in the kidney by reflex nervous activity, since the typical renal functional pattern appears in the denervated organ.⁷⁸ Moreover, fever per se is not necessary. Maintenance of a normal body temperature by antipyretic drugs does not influence the renal or systemic hemodynamic response.⁷⁴

Fever in the course of acute infections, on the other hand, is a manifestation of a highly complex situation in which renal and systemic hemodynamic alterations are complicated by water and electrolyte losses and by toxemia. The mechanism of shock and renal insufficiency appearing under these circumstances is obscure. The demonstration that marked dehydration and salt loss occur during artificial fever^{79, 80} indicates the possible operation of these factors in addition to the hemodynamic factors described above. Menkin⁸¹ has shown that certain highly toxic substances, produced locally at sites of inflammation, may enter the blood stream and cause damage in more remote areas. He suggests that necrosin, an injurious euglobulin fraction of inflammatory exudate detectable in the blood of animals with acute infections, may play a role in the production of fever. Since intravenous injection of necrosin produces focal areas of damage in visceral organs, it may also be involved in the production of renal lesions in fever. Evidence of such direct damage may be found in hematuria, cylindruria and proteinuria that appear at the fastigium of the fever, associated with the pathologic changes of acute focal nonembolic glomerulonephritis or, when less severe, with cloudy swelling of tubular epithelium. Likewise, damage by toxins may ac-

count for the curious lesions found in the adrenal cortex in the course of acute febrile illnesses. Rich⁸² remarks that these lesions, characterized by focal necrosis of the cells of the cords of the zona fasciculata with conversion of the cords into hollow tubes as a result of fluid exudation, may indicate an adrenocortical basis for circulatory collapse. In addition to the dehydration, demineralization, toxemia and shock of fever, increased tissue protein catabolism may play a role in the pathogenesis of azotemia.

Hepatorenal Syndrome

A voluminous literature has appeared in recent years regarding the so-called "hepatorenal syndrome." In the main, two viewpoints have evolved. On the one hand, it is claimed⁸³⁻⁸⁵ that, following biliary or hepatic surgery, thyroidectomy or extensive gastrointestinal operations, a profound derangement of liver function may result in "liver death," a rapidly fatal condition characterized by high fever, coma and, usually, shock. If the course is less rapid, renal damage results and death occurs in uremia associated with jaundice and other signs of hepatic failure—the hepatorenal syndrome. The proponents of the opposing view believe that "liver death" is a condition *sui generis*,⁸⁶⁻⁸⁸ attributable in most cases to overwhelming sepsis or to some obscure infection such as subphrenic abscess rather than to hepatic dysfunction. Both agree that the kidneys are damaged by toxins that may be released from the damaged liver or that may accumulate in the blood in the absence of the hepatic route of removal. Unfortunately, extensive investigation has thus far proved impossible since the disorder occurs infrequently. Case studies, for the most part, are incomplete both regarding pathological studies and regarding clinical analyses of cardiovascular, renal and hepatic function.

Renal functional impairment and hepatic dysfunction may appear simultaneously in many conditions. These include intoxication by a variety of substances (heavy metals, chloroform, cinchophen, dioxane, diethylene glycol and carbon tetrachloride),⁸⁸ septicemia,⁸⁸ certain specific diseases (Weil's disease and yellow fever), liver trauma,⁸¹ Waterhouse-Friderichsen syndrome,⁸⁹ fever therapy⁹⁰ and profound disorders of the liver (subacute yellow atrophy) and of the kidney (pyelonephritis).⁸⁸ Moreover, cases of acute diffuse glomerulonephritis or acute interstitial nephritis complicating the course of liver disease or that of infectious disease associated with jaundice may have been reported as

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ases of the hepatorenal syndrome. Obviously, several factors may be at work in any of these conditions. A common factor appears to be lacking.

Peripheral circulatory failure occurs frequently but is difficult to assess. Certain experimental work⁵⁶ and clinical experience⁹¹⁻⁹² support the notion that hepatic damage may occur in shock. Special factors, however, apart from the circulatory changes, may be involved. Mirsky and Freis⁹³ claim that trypsin injected intravenously in animals causes destructive lesions in the kidneys and liver, and they suggest that the release of similar proteolytic enzymes from damaged tissues may be responsible for the lesions observed in man. This explanation may indeed explain the findings in shock produced in animals by introducing minced meat or tissue extracts into the peritoneal cavity. The difficulty of establishing the hepatic action of such a toxin in shock, however, is illustrated by the dispute regarding the hepatotoxic effects of burns. Hepatic lesions found in fatal cases of burns have been ascribed by many workers to toxins released at the burned site,⁹¹⁻⁹² but recent work has suggested that these hepatic lesions are due, in most cases, to tannic acid, which is widely used in the treatment of burns.⁹⁴ Moreover, careful study of pathologic material from cases of fatal burns not treated with tannic acid at the Johns Hopkins Hospital and the Duke Hospital failed to show hepatic necrosis.⁹⁵ It is noteworthy, however, that in 3 of the 6 fatal cases of "traumatic uremia" reported by Darmady et al⁴³ the patients were jaundiced at the time of death.

The most important question that is raised by the hepatorenal syndrome is whether liver damage per se gives rise to renal functional and structural derangement. Unfortunately, little experimental work has been done in this direction. Animal experiments, on the whole, have been poorly controlled and are inconclusive because such variables as shock, dehydration and fever have not been properly excluded. Boyce⁸⁵ observed combined liver-kidney symptomatology in 5 dogs following release of biliary obstruction of twelve to fifty-two days' duration, and he found degenerative lesions in the livers and kidneys of dogs treated with aqueous extracts of the liver of two patients who had died in hyperpyrexia and coma ("liver death") following cholecystectomy. Experimental evidence that the liver may be concerned, in association with the kidneys, with the regulation of water and electrolyte balances has been published,⁹⁶⁻⁹⁸ but this work needs extension and confirmation. It is generally inferred that the failure of hepatic detoxifying mechanisms permits the appearance of nephrotoxic agents in the blood, but this opinion, also, lacks experimental proof. Finally, there is disagreement regarding the effect of jaundice on kidney function. In 16 jaundiced patients, Elsom⁹⁹ found urinary signs of renal damage that cleared with disappearance of the icterus. In infants with long-sustained

and uncomplicated jaundice due to congenital atresia of the bile ducts, renal lesions consisting of focal exudative changes and tubular casts have been observed in the absence of any renal functional impairment.¹⁰⁰

In short, a definitive organization of the data and a clear-cut description of events in the hepatorenal syndrome cannot yet be formulated. The term appears to embrace a large group of diverse entities and may be used correctly only in a descriptive clinical sense.

Vomiting

Vomiting is a cause of dehydration not only because gastric secretions are lost but also because fluid cannot easily be replaced. When vomiting is associated with pyloric obstruction, the loss of the hydrochloric acid rapidly produces a relative increase of base, with alkalosis.²⁹ Ultimately, if intestinal secretion is also lost in the vomitus, or if acid production lessens, the loss of base may become excessive and acidosis develops.²⁹ Regardless of the state of the acid-base balance, however, this process of electrolyte and water loss may be complicated by nitrogen retention and, finally, by the clinical manifestations of uremia. Brown, Eusterman, Hartman and Rowntree¹⁰¹ appear to have first described the renal lesions appearing in this state. In 6 of 11 cases showing signs of uremia, necropsy revealed evidence of nephrosis or acute nephritis. McLetchie¹⁰² has recently pointed out the resemblance of the lesion to that seen in the crush syndrome. Again it seems probable that reduction of the renal blood flow and glomerular filtration are responsible,¹⁰³ although extensive studies of renal hemodynamics have not been made. Clausen¹⁰⁴ has found that nausea and vomiting alone may induce transient reduction of the filtration rate, but it is not unlikely that this phenomenon is related to the effect of increased intra-abdominal pressure¹⁰⁵ during vomiting. Herrin¹⁰⁶ claims that increased urea production is not a factor in causing the azotemia. Consequently it seems not unlikely that urea is retained as a result of filtration deficiency, and it is possible that renal ischemia produces lesions akin to those of shock. The question of hypochloremia in the pathogenesis of renal functional impairment has been discussed above.

Alkalosis

Although it seems agreed that the renal changes following protracted vomiting are not necessarily related to the acid-base balance of the blood, the use of alkalis in the treatment of peptic ulcer has directed the attention of medical men to the syndrome of azotemia, hyposthenuria and alkalemia that appears occasionally in the course of alkali therapy. Hardt and Rivers¹⁰⁷ are generally credited with the first detailed description of alkalosis. In their study,

some 6 cases were reported in which clinical evidence of renal damage was apparent. The kidneys of one were found to contain scattered focal glomerular lesions. The clinical picture described by Hardt and Rivers has since been frequently reported, and the concept that alkali therapy is in some manner responsible has taken root. Additional necropsy findings have been reported, but lack consistency. Cooke¹⁰⁸ described an "acute interstitial nephritis," Oakley,¹⁰⁹ focal fatty degeneration of the tubular epithelium, and Nicol,¹¹⁰ congestive medullary changes with tiny fat granules in the epithelial cells, whereas Kirsner et al.¹¹¹ could find no changes clearly attributable to alkalosis or prolonged alkali therapy. Several cases have been described in which renal functional impairment, in terms of hyposthenuria, microscopic hematuria, proteinuria and decreased urea clearance persisted for a long period following discontinuance of alkali therapy.^{28, 112, 113}

Nicol¹¹⁰ was impressed with the fact that renal functional alteration and alkalosis in his series were uniformly associated with dehydration. Alkalosis in the absence of dehydration failed to evoke azotemia, and he concluded that dehydration held a fundamental etiologic position in the picture. Moreover, he and others¹⁰³ failed to confirm Cope's¹¹⁴ finding that magnesium and other bases were increased, and he concludes that Cope's "alkali poisoning," if it occurs at all, is decidedly unusual. Addis and his co-workers¹¹⁵ found that such an alkali poisoning caused hematuria in rats, but Kirsner¹¹⁶ failed to detect any renal damage in dogs following massive doses of alkali, except occasional insignificant calcification. A thorough study of one case by McCance and Widdowson¹⁰³ revealed marked depression of the glomerular filtration rate and disorganization of tubular function. Persistent acidity of the urine (despite alkalosis), hyposthenuria and various errors of excretion appear to resemble those of renal insufficiency in all forms of renal disorder, functional or structural. Further studies of the renal functional effects of alkali therapy are needed, however, to clarify the relative importance of dehydration and intrinsic renal damage by alkalosis in the production of the clinical syndrome.

It is particularly important to know definitely whether pre-existent or intercurrent renal disease is accelerated or stimulated to activity by alkali therapy. Victims of renal disease do not tolerate alkalis well, rapidly developing alkalosis after relatively small doses, because the kidneys fail to excrete base with sufficient rapidity to maintain plasma composition.¹¹⁷ It is possible that occasionally such patients, with unrecognized pre-existent renal disease, have been reported as cases of azotemia due to alkalosis. Certainly, either direct renal damage by alkali or unrecognized, concurrent or pre-existent renal disease must be called on to explain the course of events in certain patients in

whom dehydration appears to have been ruled out as a factor.

Hematemesis

When vomiting is associated with bleeding into the gastrointestinal canal, azotemia almost always appears. General agreement regarding the mechanism of this azotemia has not been reached. Black¹¹⁸ and Johnson¹¹⁹ have studied the kidney function in man by clearance methods shortly after hematemesis and have observed marked depression of the glomerular filtration rate. Although they admit that absorption of nitrogen from blood digested in the bowels and increased urea production by tissue breakdown may accentuate the nitrogen retention, they agree that the impaired renal function appears to be secondary to the hypotension resulting from blood loss and dehydration. On the other hand, a large group of workers, including Stevens, Schiff, Lublin and Garber,¹²⁰ Chunn and Harkins¹²¹ and Yuile and Hawkins,¹²² have failed to observe any significant change in renal function following hematemesis. They claim that excess intake of nitrogen, derived from digested blood in the gastrointestinal tract, is sufficient to account for the elevated blood urea concentration. The extent of the azotemia appears to be related to the volume of blood lost, and there is evidence that similar blood levels of urea are attained following the feeding of blood to animals. The latter claim is denied by Black¹¹⁸ and by Gregory et al.¹²³ It is probably true, however, that renal function is impaired if hemorrhage causes any degree of peripheral circulatory collapse. Hence, it is not at all unlikely that the assertions of both groups are well founded and that hemodynamic, alimentary and metabolic factors contribute in varying degree to the azotemia after hematemesis.

Diarrhea

Water loss in diarrhea results in shock and extra renal uremia as quickly as does water loss through any other portal. In this instance, however, acidosis is the rule because alkaline intestinal secretions are discharged in large volume.²⁹ Rarely, alkalosis may develop.^{124, 125} It is unlikely that acidosis per se causes renal dysfunction.³⁷ Dehydration is undoubtedly of prime importance, a fact implicit in the recognition, over a period of more than one hundred years, that salt and water replacement is the treatment of choice.¹²⁶

Adrenocortical Insufficiency

The crisis of Addison's disease (acute adrenocortical insufficiency) is characterized by the tachycardia, hypotension, cyanosis and cold clammy extremities of peripheral circulatory collapse and, like that condition, has been shown to arise from a marked reduction in plasma volume.¹²⁷ Evidence of

impaired renal function may be prominent. Azotemia and hyposthenuria give evidence of renal insufficiency, and a considerable body of experimental work indicates that renal functional incapacity may figure prominently both as a cause and a consequence of the Addisonian crisis. Renal tubular reabsorption of sodium is impaired as a result of the absence of adrenocortical secretions, and sodium and water are lost in excess in the urine.¹²⁵ Loeb and his colleagues¹²⁷ have shown that crisis may be precipitated by withdrawing sodium from the diet of patients with Addison's disease. Extracellular water is also reduced by a shift of fluid into the intracellular spaces in the adjustment of osmotic-pressure differences.¹²⁹ Other renal tubular dysfunctions are produced by adrenal insufficiency. Potassium excretion is impaired because glomerular filtration rate is reduced while tubular reabsorption is increased; this raises the potassium content of the intracellular and extracellular fluids.¹²⁸ Diminished ammonia formation, despite the need for base conservation, has been cited as a possible cause for the sodium deficiency.¹³⁰ It is not clear whether water reabsorption is also affected. It has been suggested that the hypophyseal-hypothalamic mechanisms may be disturbed as a result of adrenal disease and that the salt and water balances may be influenced primarily by this factor.¹³¹ Evidence of pituitary involvement, however, is conflicting,^{132, 133} and no defect of water reabsorption has been noted in man.⁴¹ It seems likely that azotemia is primarily a result of the reduction in glomerular filtration that has been demonstrated under these circumstances,¹²⁸ which is attributable in part to systemic circulatory inadequacy. Restoration of the sodium content of the body fluids of adrenalectomized dogs by the parenteral administration of hypertonic saline solutions corrects the impairment of filtration rate and urea excretion but does not improve potassium excretion and tubular sodium reabsorption.¹²⁵

Although it is likely that systemic circulatory changes play a dominant role in the renal insufficiency of the Addisonian crisis, persistent renal hemodynamic alterations, demonstrable during intercritical periods, must be based on other as yet undefined factors. Talbott et al.⁴¹ have found that the glomerular filtration rate and the renal blood flow tend to be reduced despite specific hormone therapy and in the absence of the usual clinical signs of renal insufficiency. Filtration is reduced relatively more than blood flow. This abnormality appears to be functional, since renal pathology specifically attributable to adrenocortical insufficiency has not been observed.^{41, 134, 135} When structural changes are found in the kidneys they appear to be secondary to other disease processes, such as pyelonephritis, or to shock. Talbott suggests that the pathogenesis of the renal impairment of Addison's disease may be multiple rather than single. It is regrettable that

hematologic studies are not mentioned in this excellent study, since anemia can produce in its own right an identical renal functional pattern.³⁹

Diabetic Coma

A considerable body of evidence is available that azotemia occurs commonly in diabetic coma.^{136, 137} The loss of water and base during glucose diuresis and the renal excretion of acidic metabolites of diabetes lead ultimately to dehydration and coma. In this situation the retention of urea and other nitrogenous products on the basis of reduced glomerular filtration rate is to be expected. There is, however, much evidence that renal function may be perverted during convalescence even when coma has been satisfactorily treated.¹³⁷ These abnormalities of function include a reduction of glucose excretion and decreased inulin, creatinine and urea clearances.¹³⁸ Marked sodium loss occurs despite an intact ammonia-producing mechanism. Following a study of this condition, McCance and Lawrence¹³⁷ state that dehydration, hypotension or urea overproduction could not be solely responsible in many of their cases. Blood volume was not measured, however, and the possibility that underlying specific renal pathology might have been responsible was not recognized.

The following year, Kimmelstiel and Wilson¹³⁹ described a renal lesion — intercapillary glomerulosclerosis — apparently typical of diabetes mellitus. This lesion, consisting of collections of a dense hyaline material in the glomeruli between capillary loops, has been found in the kidneys of from 44 to 64 per cent of diabetic patients, according to recent studies.^{140, 141} Specificity is claimed, but this point remains disputed.¹⁴² Such a glomerular lesion probably interferes with filtration and, in association with protein loss through the damaged capillary walls, leads ultimately to the simultaneous appearance of the nephrotic syndrome and uremia. Earlier in the disease process it may well account for the signs of renal damage, apart from coma, described by McCance and Lawrence¹³⁷ and others.¹³⁸

Congestive Heart Failure

All the disorders thus far discussed have in common, at some time or other in their course, a reduction in the effective circulating plasma volume. It is difficult to evoke a similar mechanism to explain the renal insufficiency of congestive heart failure, which is manifested in proteinuria, cylindruria, microscopic hematuria and azotemia. The urinary specific gravity is usually high, although hyposthenuria may occur.^{143, 144} As in Addison's disease and in diabetes mellitus, there are two phases to be considered — an acute stage in which decompensation first occurs and the phase of chronic decompensation.

In the first phase, it is generally held that so-called "backward failure" of the heart results in an increased venous pressure,^{143, 144} which upsets the balance of forces across the capillaries throughout the body. The expansion of the volume of interstitial fluid or edema that follows must occur at the expense of the circulating plasma volume. In this situation, a state similar to dehydration might produce an apparent renal functional impairment as a result of the renal response to hemoconcentration. Highly concentrated urine would be formed, with the retention of water, salt and nitrogen until the plasma volume had returned to a more nearly normal value. This process might be expected to continue until the forces operating across the capillary wall were adjusted by an increase in tissue tension. Unfortunately, the physiology of acute congestive heart failure has not been fully studied, and experimental evidence for this concept is not complete.

In chronic or slowly developing decompensation, the fact that plasma volume is increased,^{143, 144} together with evidence of renal retention of salt and water on some basis other than hemoconcentration, has focused attention on the possibility that renal dysfunction may be present in this state and operative, perhaps, throughout the entire course of the disorder.^{145, 146} It has been suggested that the increased venous pressure in heart failure may be caused by an expansion in plasma volume secondary to renal retention of salt and water.¹⁴⁶

The cause of the renal functional impairment in cardiac decompensation is obscure. There is evidence that renal circulatory changes occur. Seymour and his associates¹⁴⁷ claim, on the basis of clearance studies in man, that renal blood flow is reduced, probably in part by active renal vasoconstriction. It seems unlikely that a reduction in cardiac output is a contributing cause of renal ischemia, since McMichael and Sharpey-Schafer,¹⁴⁸ in a careful study, failed to find a consistent directional change in the output of the heart. Increased venous pressure may be a cause of the decreased blood flow, as it is in the extremities.¹⁴⁹ The renal blood flow seems to be reduced more than the glomerular filtration rate,¹⁴⁷ a functional pattern identical with that of essential hypertension.¹⁵⁰ It is difficult to see how this hemodynamic pattern can be held accountable for water retention, since even more profound changes may occur in the course of hypertension without the development of edema. The reduction in glomerular filtration rate is not usually striking.¹⁴⁷ Consequently, it seems unlikely that glomerulotubular imbalance such that filtrate formation decreases relative to the tubular capacity for water and salt reabsorption is responsible for retention, as it may be in acute diffuse glomerulonephritis.¹⁰ This possibility, however, has not been fully investigated. Since failure is often superimposed on what appear to be otherwise normal

kidneys, filtration reduction — such as it is — may be ample to bring this mechanism into play. Fishberg¹⁴⁴ emphasizes the degree of renal congestion that occurs in decompensation, and it is possible that venous congestion with resulting increase in intrarenal pressure is implicated in the reduction of blood flow and filtration. Increased renal venous pressure, intrarenal tissue tension¹⁵¹ and intra-abdominal pressure¹⁵² are known to produce increased concentration of the urine regardless of the state of hydration. It may be that similar factors are at work in heart failure and that renal dysfunction is a result rather than a cause of increased venous pressure.

* * *

It is obvious that renal insufficiency in any single patient is compounded of many diverse elements. Careful analysis is imperative in each case, since many types of renal failure are reversible and amenable to treatment. These are perhaps best illustrated by the renal insufficiencies of urologic practice. In these conditions, kidney damage and renal functional impairment secondary to urinary-tract obstruction frequently coexist. Surgical correction of obstruction may be lifesaving despite the presence of a profound uremia.¹⁵² It is equally true that extrarenal factors that can be corrected may be at work in many cases of uremia resulting primarily from intrinsic renal disease. Treatment of dehydration, congestive heart failure and the like may result in striking clinical improvement without a parallel improvement in the basic renal pathology. Every case of uremia deserves close attention and vigorous treatment, since "watchful procrastination" may be fatal.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

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CASE 31441

PRESENTATION OF CASE

First admission A thirty-one-year-old woman entered the hospital complaining of intermittent sharp pain low in the back and abdomen

Three and a half months before admission the patient was exposed to extremely cold weather during a menstrual period. A few hours later she noticed that the flow had ceased. She had chills and became very weak. These symptoms continued during the night, and when she arose the next morning she noticed fecal incontinence. A day later she had cramping pain low in the abdomen but there was no vaginal bleeding, nausea or vomiting. Her local physician prescribed an ice bag and sulfathiazole. In about a week she felt well enough to get up. Within a few days, however, the low abdominal pain again appeared. After this initial attack, similar pain recurred with increased frequency. Her menses had begun at the age of twelve, they occurred regularly every twenty-eight days, with a six-day flow of normal amount. Since their onset, she had always had pain in the right lower abdomen just prior to flow. Her periods became somewhat more frequent following the onset of her illness, and the recently originating abdominal pain often came on just as the flow ceased. At first the pain was severer on the right than on the left, but later it shifted to the left side, radiating down the groin to the external genitalia. She lost 20 pounds and became weak. One month before admission her physician drained a mass in the left lower quadrant through the vagina, obtaining clear fluid and mucus. A mass was also found in the right lower quadrant, but nothing was done about it. At about that time, for a short period, she noticed a severe pain in the sacrum. During the three days before admission this pain recurred, and she had urgency and frequency of urination. Nocturia had been present for several years.

Since the birth of her only child, six years before admission, she had had a yellow mucoid discharge. Two years before admission she had "pleurisy," with severe chest pain on inspiration, which subsided in three days. She did not get along well with her husband and had indulged in extramarital sexual relations.

*On leave of absence

Physical examination revealed a well developed, well nourished young woman in acute distress. The breasts were normal. The tonsils were large and infected. The lungs were clear. The heart was of normal size. An apical systolic murmur was heard. The spleen and liver were not palpable. In the right lower quadrant of the abdomen was a large, tender, firm, smooth, oval-shaped mass extending to the midline. On pelvic examination, the cervix showed a transverse laceration, with a white discharge exuding from the external os. Both right and left vaults were filled with a firm mass.

The temperature was 101°F, the pulse 100, and the respirations 20. The blood pressure was 120 systolic, 75 diastolic.

Examination of the blood showed a white-cell count of 16,800. The urine was normal. A smear of the cervical discharge was negative for gonococci. A chest plate showed no evidence of active lung disease.

Three days after admission vaginal bleeding began. Penicillin (96,000 units) was given intramuscularly daily for twelve days, and her condition improved. She was discharged on the nineteenth hospital day.

Second admission (four months later) After discharge the patient was followed in the Out Patient Department. She had no complaints except for frequency of urination and a sensation of pressure on the bladder and rectum. An intravenous pyelogram showed normal bones and joints of the lumbar spine and pelvis. The psoas shadows were symmetrical. A large soft-tissue mass occupied the pelvis and extended to the upper margin of the sacrum. The liver and spleen were not remarkable. The kidneys appeared somewhat larger than usual but were normal in position. The intravenous dye was delayed in appearance and poor in concentration, outlining dilated calyces, pelves and ureters bilaterally. The dye was better concentrated on the left than on the right. The flattened bladder was barely visible at the base of the pelvic mass. Repeated vaginal smears for malignant cells were negative. One month before admission the patient had a menstrual period at her regular time. The flow was normal, and there was not much pain. A week after cessation of flow, which had lasted for eight days, slight vaginal bleeding was noted, which continued until readmission. There had been no weight loss.

Physical examination revealed the patient to be well developed and well nourished and in no discomfort. The heart and lungs were normal except for an apical systolic murmur. Pelvic examination revealed a normal cervix. The uterus was displaced forward. A large mass occupied both sides of the pelvis. On the right, the mass was cystic, and on the left, fixed and immovable.

The temperature was 98.6°F, the pulse 80, and the respirations 20. The blood pressure was 130 systolic, 90 diastolic.

The urine was normal. The white-cell count was 6,400, with 75 per cent neutrophils. The hemoglobin was 9.5 gm per 100 cc. An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD HAMLIN: May we see the x-ray films?
DR. MILFORD D. SCHULZ: The films of the chest show nothing significant except for an old healed primary tuberculous complex. Excretory urograms show a large soft-tissue mass arising out of the pelvis, its edges cannot be defined. The dye given intravenously was excreted slowly, best visualization occurring at the end of an hour, when large dilated calyces, pelvis and ureters are shown, better on the left side than on the right, that is, there was bilateral hydronephrosis, with obstruction low in the ureters, probably due to a pelvic mass. The nature of the mass cannot be determined. There is no calcification within it, such as is sometimes seen with papillary carcinoma of the ovary.

DR. HAMLIN: This is a relatively young woman on whom it seems probable that the person who wrote out the abstract wanted me to make a diagnosis of pelvic inflammatory disease, and on whom it seems clear that the house staff on admission made that diagnosis, and indeed I find it difficult to get away from the diagnosis of pelvic inflammatory disease. She had a large mass in the pelvis over a period of several months, which certainly on the first admission gave every evidence of being acutely inflamed. Apparently it produced obstruction to the renal outflow, with the formation of hydro-ureters, and presumably she eventually had the tumor removed.

In going over the protocol, the first thing that interested me was the history of the onset of this illness, which began when she was exposed to extremely cold weather during the menstrual period. I had always believed that the harm resulting from exposure to cold and bathing in cold water at such a time was more or less an "old wives' tale" rather than a physiologic idea, and I still believe so. Very likely that was not the cause of her trouble.

The personality of this woman was such that one might readily expect a Neisserian infection or even an abortion, so that these two possibilities must be kept in mind. The fact that she had chills at the onset perhaps makes it a little unlikely that this was purely a gonococcal infection. Chills are relatively infrequent in gonococcal salpingitis and are far likelier to be associated with a septic abortion. In any event, I believe that she developed infection in the pelvic organs, producing acute endometritis, salpingitis and oöphoritis, with large tubo-ovarian abscesses. Her local physician tapped one of these masses through the vagina and obtained colorless serum and mucus. That may seem inconsistent with a tubo-ovarian abscess, because usually the purulent abscess takes a far longer time to become sterile

and clear itself of debris than had elapsed here. Nevertheless, the associated inflammation in the pelvic peritoneum might well produce such encapsulated masses of fluid that could have been drained.

The fecal incontinence associated with the onset of her illness can probably be explained by pelvic peritonitis irritating the sigmoid. This may occur in a pelvic peritonitis associated with appendicitis or with any other such type of infection.

Of course, she could have had some pelvic abnormality that antedated the onset of the illness, such as an ovarian cyst of one sort or another, which might have become infarcted by twisting. There is no sound basis for this consideration, however, and I shall dispense with it.

She could have had many different types of infection. I suppose one should think of tuberculosis, which is said to occur in a little more than 5 per cent of all cases of pelvic inflammatory disease. She had had pleurisy in the past, but the chest films were clear, and it is rare to have tuberculosis present in the pelvic organs without associated tuberculosis elsewhere, of which there was no evidence. Actinomycosis is a rare infection in the pelvic organs, but it may occur. If it occurred in this case, the patient certainly had a secondary infection associated with it. I see no reason to consider it further. There are many other vague possibilities, but I cannot get away from the fact that to me this appears to be a fairly typical history of pelvic inflammatory disease, following what I should say was a reasonably characteristic course.

A PHYSICIAN: How about pregnancy?

DR. HAMLIN: I suppose that one can never rule out pregnancy without an Aschheim-Zondek test.

A PHYSICIAN: How about an extrauterine pregnancy?

DR. HAMLIN: It is a possibility, but to my mind the sequence of events does not give it a great deal of weight.

A PHYSICIAN: How can you rule out a pseudomucinous cyst so easily?

DR. HAMLIN: I cannot rule it out, but there is no indication that she had one. If she did have one, there must have been an associated infection.

DR. RONALD C. SNIFFEN: Do you mean a malignant cyst?

A PHYSICIAN: No, I thought that perhaps the evidence of infection could have been due to a twisting of the pedicle of a cyst or to hemorrhage occurring within it that set up a foreign-body reaction.

DR. HAMLIN: I mentioned that briefly.

DR. FREDERICK A. SIMMONS: When this patient first came to my attention the history was that of inflammatory disease. The temperature varied from 98 to 104°F, but it came down on penicillin and she was discharged from the hospital. I shall read the note that I wrote at that time.

This thirty-one-year-old patient has no complaints, except for a feeling of pressure on the bladder and in the

rectum. She is able to do her work and instead of losing weight may be gaining slightly. She looks well and healthy, yet she has a large, smooth, midline suprapubic mass extending three fingers above the symphysis. It is fixed and nontender. On pelvic examination there is a marital introitus, a normal-feeling cervix, which is slightly hypertrophied, and a uterus that seems anterior. The mass, in my opinion, is attached to but is not a part of the uterus and extends superiorly, laterally and posteriorly from the cervix. It also impinges markedly on the rectum, and both broad ligaments are fixed. I believe that all the disease is inflammatory and that the mass could be removed only with great difficulty, since there is little mobility. Malignant disease, however, cannot be ruled out, and it is my impression that it would be wise to admit this patient for exploratory laparotomy.

The patient returned to the Tumor Clinic three weeks later, and at that time she obviously had a tumor, so we admitted her at once. Dr. J. V. Meigs saw the patient a day or two before operation and said "The diagnosis lies between pelvic inflammation of some sort, possibly tuberculosis, and malignant disease. I think that she ought to be explored."

CLINICAL DIAGNOSES

Pelvic inflammatory disease
Malignant tumor?

DR. HAMLIN'S DIAGNOSIS

Pelvic inflammatory disease

ANATOMICAL DIAGNOSIS

Acute and chronic salpingo-oophoritis, with
bilateral tubo-ovarian abscesses

PATHOLOGICAL DISCUSSION

DR. SIMMONS: An exploratory laparotomy was performed, and on opening the cavity we could not identify the various structures. There was a large mass in the pelvis, which I believed to be retroperitoneal. With careful dissection we were able to identify the left round ligament. The uterus appeared to be of normal size, with enormous masses in both vaults consisting of the tubes and ovarian cysts, which extended into the pouch of Douglas. The ovaries were intimately adherent to the neighboring structures. The whole pelvis was "frozen," and contained a large amount of pus. The cecum lay inside the pelvis behind the tubo-ovarian mass. The appendix was small, fibrous and apparently obliterated. Its tip, which lay against the inflammatory mass, was injected and necrotic; it was not removed. The appendix may have been the cause of the whole process. The reason I mention this possibility is that I recently operated on a patient, forty-three years old, with the same physical findings and the same history but whose personality was such that I did not believe that she had been exposed to the gonococcus. She had an appendix that had previously perforated.

DR. SNIFFEN: What is your management of patients with acute salpingo-oophoritis?

DR. SIMMONS: Just what she had during the first admission — bed rest. In extremely ill patients we frequently put down a Miller-Abbott tube, give parenteral fluids and sulfadiazine and wait until they quiet down.

DR. SNIFFEN: As Dr. Simmons has indicated this patient had a normal uterus. The tubes were large, thickened and tortuous. Their walls were at least 1 cm. in thickness and were fibrotic. The lumens were dilated to about 6 mm. in diameter and contained frankly purulent, hemorrhagic material. Each tube was sealed off at its end, and at each end there was a unilocular cyst roughly 7 cm. in diameter with thick walls that enclosed the same type of purulent material. The organisms cultured from the exudate were *Staphylococcus aureus* and nonhemolytic streptococci.

CASE 31442

PRESENTATION OF CASE

At the age of sixty-nine, the patient, a business executive, consulted his physician for a routine checkup after he had noted dyspnea on moderate exertion. At that time his blood pressure was 220 systolic, 140 diastolic, and physical examination and fluoroscopy showed that the heart was moderately enlarged in the region of the left ventricle. The aorta was tortuous, but there was no congestion of the lungs. An electrocardiogram showed evidence of slight left-axis deviation. The urine contained a small amount of albumin.

Eighteen months later he first noticed substernal pressure on effort. This sensation increased in severity for six months, at the end of which period attacks of substernal oppression appeared when the patient was at rest, with radiation of mild pain down both arms and into the jaw. The blood pressure was 235 systolic, 145 diastolic. An electrocardiogram showed normal rhythm, a rate of 90, a normal ST segment, a low T₁, a small R₄, and a high T₄.

After ten days of brief attacks of substernal oppression at rest he suffered an attack that began at 5:00 a.m. and lasted all day. Two days later he was admitted to the hospital. An electrocardiogram on admission showed normal rhythm, a rate of 80, an extremely low T₁, inverted T₂ and T₃, and a normal T₄. There was slight elevation of the ST segment in Lead 3 and slight depression in Lead 4. The white-cell count was 11,000, and the sedimentation rate 44 mm. per hour. There was no record of fever, and his convalescence was uneventful. He was discharged improved on the thirty-fifth hospital day.

After discharge from the hospital he felt well and complained of no pain. During the following year his blood pressure remained at 220 systolic, 145

astolic, and repeated fluoroscopic examinations showed that the heart and aorta were becoming progressively more enlarged. He complained of insomnia and orthopnea. Slight edema of the ankles developed, and gallop rhythm appeared. The signs of congestive heart failure became more pronounced, with variations.

At the age of seventy-two he abruptly lost almost the entire left lateral field of vision, and although his condition improved somewhat, he never recovered normal sight. He had lost the right eye in childhood in an accident.

At the age of seventy-three, four years after he was first seen by his physician, and while he was receiving much medical attention for congestive heart failure, which was held in check but never completely controlled, he suddenly complained one evening of severe pain in the small of the back and started to go to bed. Five minutes later he cried out briefly and was found dead a moment later.

DIFFERENTIAL DIAGNOSIS

DR. GREENE FITZHUGH: To summarize, we have a man with marked hypertensive cardiovascular disease, which we know had existed for four years and undoubtedly for some time longer. Two and a half years before death he began having angina pectoris, and six months later he had what I think we have to interpret as coronary thrombosis. One year before his sudden death he lost the left lateral field of vision. We are told nothing about the physical signs at the time of death. All we know is that he had one symptom — severe pain in the small of the back — and that he was then found dead. We have to theorize on the physical signs, consider the causes of sudden death and, from the history, pick out the things that will lead to a diagnosis. We might first look at the x-ray films.

DR. MILFORD D. SCHULZ: The cardiac shadow is markedly enlarged in the region of the left ventricle. The aorta is tortuous and somewhat dilated. The findings in the chest are otherwise not unusual for a patient of this age.

DR. FITZHUGH: Was there any erosion of the vertebrae?

DR. SCHULZ: You are undoubtedly thinking of an aneurysm, but there is no evidence of such on this film of the chest. The aorta can be traced almost down to the diaphragm.

DR. FITZHUGH: Aneurysms often erode the vertebrae in the thoracic and abdominal regions. The aorta is distinctly wide, which fits in with the cardiovascular disease and marked hypertension.

Let us go over the causes of sudden death. I shall name what is reasonable and see if I can pick up a lead.

We know that this patient had had one attack of coronary thrombosis. The third electrocardiogram taken showed a rate of 80, a low T_1 and so forth. In addition, he had a slight elevation of the ST

segment in Lead 3 and a slight depression of the ST segment in Lead 4. These findings, along with the story of severe pain coming at 5:00 o'clock in the morning and lasting all day, with an increased sedimentation rate and a white-cell count of 11,000, make one certain of coronary thrombosis. So it is fair to say that two years before death he had an attack of coronary thrombosis. It is not uncommon for a patient to have a second attack one to three years later, and this would not be an unreasonable final diagnosis.

The patient had had several vascular accidents, and we have to consider whether he had a vascular cerebral accident that suddenly caused death. Massive cerebral hemorrhage into the ventricle will cause sudden exitus. But there are no physical signs to go on, and with something of that nature, there should be no pain in the back. Sudden death can also result from cerebral embolism, when the supply of blood to the brain is abruptly cut off.

Another thing we should consider is a pulmonary embolus. That is a frequent cause of sudden death, particularly in a person with congestive failure, which this patient had following the attack of coronary thrombosis. Phlebothrombosis of a leg vein can suddenly produce an embolus, but there should be pain in the chest or abdomen rather than in the back. Again, we are bothered by the fact that there are no physical signs we should have liked to know whether he had dilatation of the veins of the neck. There would not have been time for an infarct to develop, and therefore, hemoptysis would not have been present.

An aneurysm of the aorta can rupture and cause sudden death, but this patient was in competent hands for four years, which means that they probably would have found a mass in the abdomen, furthermore, x-ray films of the abdomen should have shown a dilated aorta. A dissecting aneurysm of the aorta is another possibility that occurs in people with hypertension. In that condition there is often interference with circulation to the legs and, in fact, to any organ that is supplied by the aorta.

Let us review the findings to determine whether this patient simply had a second attack of coronary thrombosis. Two years before death he had pain down both arms, which is consistent with coronary thrombosis. The pain also went into the jaw, which is perfectly reasonable for an attack of angina pectoris or coronary thrombosis. As stated previously, I am sure that this man had had coronary thrombosis because of the third electrocardiogram, but I do not believe that that was the cause of his death. It is extremely unusual to have severe coronary thrombosis without pain in the chest. There can be pain in the chest or pain in the chest and abdomen, but pain solely in the abdomen or in the back usually does not occur. On the basis of this and the fact that he had had hypertensive cardiovascular disease for at least four years, I believe that this man had

a dissecting aneurysm of the aorta and that his sudden exitus was due to hemorrhage from the rupture of the aneurysm

DR CONGER WILLIAMS I had not seen this man for about a year before he died I thought that he had hypertensive coronary heart disease, with congestive failure, and also enough coronary insufficiency to cause angina I know nothing about the final episode Dr FitzHugh's explanation of the cause of death is as good as any, I should say

DR BENJAMIN CASTLEMAN Dr Wheeler, I believe that you also saw this patient

DR EDWARD WHEELER I thought that he had hypertensive heart disease and angina for some time before death and possibly coronary insufficiency for a year I did not see him in the final episode

CLINICAL DIAGNOSES

Dissecting aneurysm of aorta, with rupture
Coronary thrombosis, with myocardial infarction, old

DR FITZHUGH'S DIAGNOSES

Dissecting arteriosclerotic aneurysm of aorta, with rupture
Chronic hypertensive cardiovascular disease
Coronary thrombosis, with myocardial infarction, old

ANATOMICAL DIAGNOSES

Rupture of arteriosclerotic fusiform aneurysm of abdominal aorta
Retroperitoneal and pelvic hematoma
Arteriosclerotic aneurysms of aorta, iliac, internal carotid and cerebral arteries
Coronary thrombosis, old
Myocardial infarct, old

Cardiac hypertrophy and dilatation, hypertensive type

Arteriosclerosis, marked, generalized

PATHOLOGICAL DISCUSSION

DR CASTLEMAN The autopsy showed a tremendously enlarged heart, weighing over 800 gm, with marked hypertrophy of the left chamber, which fitted in with the longstanding hypertension The coronary arteries were markedly sclerotic and narrowed, and we were able to find evidence of old occlusion in the right one, which apparently corresponded to the old infarct in the posterior wall of the left ventricle This accounted for the episode two years before death.

On opening the abdomen we found no free fluid The intestines were raised up from the abdominal cavity, and when these were pushed aside, we discovered a large retroperitoneal hematoma, which filled the entire lower abdomen and pelvis The hematoma had been produced by rupture of a large abdominal arteriosclerotic aneurysm, — not a dissecting aneurysm but the fusiform type, — which measured about 15 cm in diameter The posterior wall of the aneurysm had ruptured just below the level of the renal artery There were smaller aneurysms in the upper abdominal aorta and both iliac arteries, such as one encounters in elderly people with severe arteriosclerosis, these are not due to syphilis This man also had two small aneurysms of the same type in the internal carotid arteries, one on each side, and smaller ones in the anterior cerebral artery, none of these had ruptured however We found nothing in the brain itself

DR FITZHUGH Was the aorta big enough to have been felt during life?

DR CASTLEMAN He was a fairly heavy-set man and it might have been difficult to detect

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RELUCTANT NAVY

SCRIBE Bill Cunningham of the picturesque pat-
ter, one of the most honest correspondents that ever
practiced shadowboxing with a typewriter, is ready
to take a fall out of any apparent injustice that
comes to his attention. This time (*Boston Herald*,
October 5) it concerns the Navy's exploitation of
the medical profession — with no Army exemption
even implied — that stirs his sympathy, the current
indictment being based on a letter received from a
medical officer now stationed in Guam and willing
to be five or six thousand miles nearer home,
practically immediately.
According to the convictions of this doctor and,
presumably, those of several thousand others, the

Navy Medical Corps is ridiculously overstaffed,
having from 30 to 50 per cent more physicians than
it has ever been able to use, with utter disregard of
the needs of the home front. The Navy, moreover,
even with relative peace brooding over the seven
seas, had indicated, according to this same inform-
ant, that it did not intend to cut down on the ratio
of one medical officer for every 233 men, to support
this profligacy it had made the discharge score for
doctors 25 per cent higher than the average for other
personnel. Since publication of the letter, however,
the score has been lowered.

This officer was burdened with daily duties, at
the date of writing, that could have been performed
by a pharmacist's mate in an hour, and he made
reference to an obstetrician assigned to inspect the
privies on the island, who, even in slow motion,
could not possibly have spent more than an equiva-
lent time on his own job — had he wished to.

There is no doubt that many of the stories that
we hear are true, and it is equally valid that when
we were actually at war, and waging a doubtful,
uphill struggle, practically no one but the Truman
Committee was willing to haggle at what our defense
cost in men, materials, money and equipment, so
long as we won and saved the Nation for the strikers.
We accepted with philosophy the presumption that
the Army, the Navy, the Air Force and the Marine
Corps would want ten times as many men as they
could put into action, ten times as much food as
those men could eat and ten times as much equip-
ment as they could use, and, like a democracy, we
gave freely. Now, with the war well won, we can
no longer tolerate the dictatorial methods of our
amazingly successful military machine — a healthy
sign, by the way — and want to dismantle it be-
fore we can get it back to the enginehouse. In-
tolerant of what seemed to many of us a reasonably
good job at demobilization after a war that was
expected to run at least another year, we have set
Congress onto the rascals, and left it running like
the hounds of spring when on winter's traces.

This is the way it is ending, and this is the way
we might even dare to hope that it will always end
if we ever have to go to war again. In Sandburg's
Abraham Lincoln is a quotation to the effect that
democracies always make war after a set pattern.

There is a lot of noise, and a lot of patriotism, and everyone expects a quick, triumphal dash to the enemy's capital and a brilliant end to the brief struggle. Instead, the conflict drags on and on, with victories and reverses, and, win or lose, everyone is thoroughly sick of it before it is over.

No matter how well organized and how successful it may be, a military machine is wasteful, dictatorial, arrogant and, at times, terribly necessary. The fact remains that when the occasion is over, militarism is simply incompatible with democracy.

Additional scuttle butt, emanating from no less an authority than Drew Pearson, credits Admiral Halsey with the following message to General MacArthur on the occasion of the latter's entrance into Tokyo, "You have hit the jack pot with my nickell!"

medical knowledge in New England. Refurnishing of quarters, additional stacks and an increased personnel, as well as the lack of funds to do many other things so urgently needed in the immediate future are all problems that must be faced in the next few years. A plan, as outlined in the president's report, calls for full co-operation of the physicians and the institutions, hospitals and medical schools to use the Library as an essential part of their equipment. The Library, a sound, splendid storehouse of medical thought in printed form, is a part of the educational and cultural system, firmly planted to the physicians of the past, that richly deserves the support of the present generation if they, as they should and must, "hold fast to that which is good."

OBITUARY

DAVID LINN EDSALL

1869-1945

THE BOSTON MEDICAL LIBRARY

THE annual reports of the president and librarian of the Boston Medical Library, as presented elsewhere in this issue of the *Journal*, merit the thoughtful consideration of physicians.

The Library, in spite of wartime restrictions, continued in 1944 to grow and to be used by an increasing number of readers, suggesting that this old and well established institution, so long supported by the medical profession in Boston and its vicinity, still serves an important function in the scholarly life of the community. The librarian reports a healthy activity in accessions, with due regard for periodical literature, the basis for current research, and the latest texts, the latter coming largely through the book-review department, closely integrated with the *Journal*. By using its endowed book funds, much new material, both old and current, was added to its shelves for the benefit of its members and the public at large.

On the basis of the librarian's summary, therefore, all would seem well with the Boston Medical Library. A reading of the president's report, however, will reveal on how slender a thread hangs the essential structure. The Library lacks a suitable financial endowment, not only to maintain itself in its present position but to expand and go forward as an important cog in the wheel of advancing

With the death of David Edsall a truly great figure passes from the scene of American medical education. During his long life he occupied full professorial rank on the medical faculties of three universities—Pennsylvania, Washington and Harvard. Large both in body and mind, with indomitable will and great breadth of vision, throughout his professional career, he pursued relentlessly his clearly perceived objectives, which were the improving of the teaching of medicine and the promotion of medical research. His success in reaching these goals makes it quite fitting to proclaim him a statesman in medicine.

After college days at Princeton (A.B. 1890), he studied medicine at the University of Pennsylvania, obtaining his degree of M.D. in 1893. He remained in Philadelphia until 1911, serving as professor of therapeutics and pharmacology from 1907 to 1911 and as professor of medicine during 1910 and 1911. His Philadelphia period was distinguished chiefly by his contributions in clinical investigation, particularly in problems of metabolism and nutrition. Most of his research in those days was carried out in the Pepper Laboratory. Quite early too, he became interested in the medical hazards of industry and how to prevent them.

His St. Louis period, during which he served as professor of preventive medicine, lasted but one year, 1911-1912, and was not particularly satisfying to him. At about that time, however, he found opportunity to work for a brief interval at the Carnegie Nutrition Laboratory in Boston, and there became keenly interested in the application of Benedict's so-called "universal respiration apparatus" to clinical problems of respiration and respira-

try metabolism In the Shattuck Lecture of 1912 e vividly sets forth his experiences and ideas in his field

It is in his Boston period, which extended from 1912, when he assumed the duties of Jackson Professor of Clinical Medicine at Harvard and of chief of the East Medical Service at the Massachusetts General Hospital, to his retirement from active work in 1935, that the readers of the *Journal* will be chiefly interested

The Boston period subdivides itself into three phases. From 1912 to 1918 his activities centered in the hospital and were concerned with the development of clinical teaching and research During that time Dr Edward H Bradford was dean of the Harvard Medical School In 1918 Dr Edsall succeeded Dr Bradford as dean, without relinquishing his earlier posts, and in 1921 he founded and became dean of the newly established Harvard School of Public Health In 1923 the third phase of his Boston period began, when he resigned from his chair of medicine and from the hospital staff Thereafter, until his retirement in 1935, he served as full-time dean of the schools of medicine and of public health

While at the Massachusetts General Hospital, Edsall greatly improved the teaching of undergraduate medical students He established there the clinical clerkship in medicine and full-time clinical teaching In contrast to the completely full-time system already started at Johns Hopkins, Edsall believed that it made for better teaching if all clinical teachers had some contact with private patients Therefore at Harvard, although clinical teachers began to receive salaries (usually paid jointly by school and hospital) for their full-time work, they were permitted to see and collect fees from a limited number of private patients This has come to be known as the "Harvard variety" of full-time clinical work Edsall further believed that medical students would be better taught if they had the opportunity to come under two types of teachers—the old voluntary group with great clinical experience and full-time teachers, who were more conversant with medical research and had more time to devote to actual teaching and academic administration He regarded a teaching hospital staff composed of both volunteer and paid members as more effective than one made up of either variety of teacher alone The passing years have proved that this was wisdom In his conduct of affairs at the hospital he never allowed himself to become bogged down by details He went after what he regarded as fundamental, at times almost ruthlessly, treading, perhaps inevitably, on a certain number of toes in the process When he had made up his mind to a course of action he hewed to the line, letting the chips fly where they might, and not minding much whom they hit

To him the medical services at the Massachusetts General Hospital are indebted for excellent clinical

research facilities, including substantial additions to the space within the Bulfinch Building He found ways and means for providing full-time salaries for young men of promise and was constantly on the lookout for such human material

During his hospital days he proved himself to be a gifted teacher In the lecture room he interested particularly the abler students He was at his best at the bedside, where he succeeded in showing that the most skillful care of the patient is that which is planned in the light of a clear understanding of the basic principles of the medical sciences involved He was able to integrate research, teaching and the care of the patient Nor was he blind to social factors The role of environment in determining the whole clinical picture was constantly apparent to him He started a clinic for the study and care of patients with illness due to occupation

After he had got full-time medicine established at the Massachusetts General Hospital he was largely instrumental, a few years later, in doing the same for surgery, and a little later still for psychiatry From his first arrival he exercised, through his membership on the General Executive Committee, a powerful influence on the policies of the hospital He aimed not only to improve its methods and physical equipment but more particularly to strengthen its staff by adding thereto physicians giving promise of productive scholarship in medicine

Edsall will live not only through his works but through his pupils Of these there were many, and they have gone to spread his gospel in many places Some of them have attained great distinction In addition to being intellectually stimulating, he had a personality that could be endearing He had a capacity for friendship that was exercised chiefly on a selected group of intimates For younger men he often had great personal attraction He had a sense of humor and twinkle in his eye, which, together with his little black brier pipe, made him, on intimate occasions, rather irresistible He loved a good story and was a fine raconteur Like all strong characters, he occasionally made enemies as well as friends

During his seventeen years as full-time dean of the Harvard Medical School and the thirteen as dean of the Harvard School of Public Health, Edsall carried over into the fields that these schools encompass the principles that he had earlier applied to clinical medicine

At the time of his arrival in Boston, the Harvard Medical School, with a brilliant past behind it, had to some degree got into the academic doldrums The school owes much to the late Dr Frederick Cheever Shattuck for taking the lead in importing fresh blood in the shape of Edsall, to start a new era And start it he did! Largely through his efforts the capital funds of the school increased from less than five million dollars in 1918 to about seventeen million dollars in 1935 He was a great money raiser Un-

There is a lot of noise, and a lot of patriotism, and everyone expects a quick, triumphal dash to the enemy's capital and a brilliant end to the brief struggle. Instead, the conflict drags on and on, with victories and reverses, and, win or lose, everyone is thoroughly sick of it before it is over.

No matter how well organized and how successful it may be, a military machine is wasteful, dictatorial, arrogant and, at times, terribly necessary. The fact remains that when the occasion is over, militarism is simply incompatible with democracy.

Additional scuttle butt, emanating from no less an authority than Drew Pearson, credits Admiral Halsey with the following message to General MacArthur on the occasion of the latter's entrance into Tokyo, "You have hit the jack pot with my nickel!"

medical knowledge in New England. Refurnishing of quarters, additional stacks and an increased personnel, as well as the lack of funds to do many other things so urgently needed in the immediate future, are all problems that must be faced in the next few years. A plan, as outlined in the president's report, calls for full co-operation of the physicians and the institutions, hospitals and medical schools that use the Library as an essential part of their equipment. The Library, a sound, splendid storehouse of medical thought in printed form, is a part of the educational and cultural system, firmly planted by physicians of the past, that richly deserves the support of the present generation if they, as they should and must, "hold fast to that which is good."

OBITUARY

DAVID LINN EDSALL

1869-1945

THE BOSTON MEDICAL LIBRARY

THE annual reports of the president and librarian of the Boston Medical Library, as presented elsewhere in this issue of the *Journal*, merit the thoughtful consideration of physicians.

The Library, in spite of wartime restrictions, continued in 1944 to grow and to be used by an increasing number of readers, suggesting that this old and well established institution, so long supported by the medical profession in Boston and its vicinity still serves an important function in the scholarly life of the community. The librarian reports a healthy activity in accessions, with due regard for periodical literature, the basis for current research, and the latest texts, the latter coming largely through the book-review department, closely integrated with the *Journal*. By using its endowed book funds, much new material, both old and current, was added to its shelves for the benefit of its members and the public at large.

On the basis of the librarian's summary, therefore, all would seem well with the Boston Medical Library. A reading of the president's report, however, will reveal on how slender a thread hangs the essential structure. The Library lacks a suitable financial endowment, not only to maintain itself in its present position but to expand and go forward as an important cog in the wheel of advancing

With the death of David Edsall a truly great figure passes from the scene of American medical education. During his long life he occupied full professional rank on the medical faculties of three universities — Pennsylvania, Washington and Harvard. Large both in body and mind, with indomitable will and great breadth of vision, throughout his professional career, he pursued relentlessly his clearly perceived objectives, which were the improving of the teaching of medicine and the promotion of medical research. His success in reaching these goals makes it quite fitting to proclaim him a statesman in medicine.

After college days at Princeton (A B 1890), he studied medicine at the University of Pennsylvania, obtaining his degree of M D in 1893. He remained in Philadelphia until 1911, serving as professor of therapeutics and pharmacology from 1907 to 1910 and as professor of medicine during 1910 and 1911. His Philadelphia period was distinguished chiefly by his contributions in clinical investigation, particularly in problems of metabolism and nutrition. Most of his research in those days was carried out in the Pepper Laboratory. Quite early too, he became interested in the medical hazards of industry and how to prevent them.

His St. Louis period, during which he served as professor of preventive medicine, lasted but one year, 1911-1912, and was not particularly satisfying to him. At about that time, however, he found opportunity to work for a brief interval at the Carnegie Nutrition Laboratory in Boston, and there became keenly interested in the application of Benedict's so-called "universal respiration apparatus" to clinical problems of respiration and respira-

Medical Corps of the Army, — January, 1944 — he was a member of the staff of the Milford Hospital. He was sent to England in July, 1944 as a member of the 101st Airborne Division, and was later transferred to the Continent. His widow, three sons, one daughter, his mother and two others survive.

MAYBERRY — Frank F. Mayberry, M.D., of Rockland, died October 1. He was in his eighty-sixth year. Dr. Mayberry received his degree from Dartmouth Medical School, Hanover, New Hampshire, in 1885. He retired in 1931. His widow, two daughters and a brother survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR SEPTEMBER 1945

DISEASES	RÉSUMÉ		
	SEPTEMBER 1945	SEPTEMBER 1944	SEVEN YEAR MEDIAN
Interior poliomyelitis	163	131	20
Ch. croup	1	1	*
Chicken pox	90	132	105
D. tetra	14	14	10
D. r. bile	940	824	882
Dysentery bacillary	11	40	29
German measles	49	30	25
Gonorrhea	405	410	419
Graciloma inguinale	0	0	*
Lymphogranuloma venereum	0	3	*
Malaria	102	26	5
Measles	145	92	150
Meningitis meningococcal	4	11	6
Meningitis Pfeiffer bacillus	1	0	0
Meningitis pneumococcal	1	1	2†
Meningitis staphylococcal	0	0	0†
Meningitis streptococcal	0	0	0†
Meningitis other forms	0	0	0†
Meningitis undetermined	1	4	4†
Mumps	194	224	150
Pneumonia lobar	57	66	114
Salmonella infections	10	13	13
Scarlet fever	190	241	240
Syphilis	292	363	403
Tuberculosis pulmonary	218	199	229
Tuberculosis other forms	14	11	23
Typhoid fever	0	2	5
Undulant fever	2	2	2
Whooping cough	268	265	405

*Made reportable December 1945.
†Four year average.

COMMENT

Interior poliomyelitis cases for September exceeded those for any month this year and probably represent the peak for the year. It can be expected from past experience that the number of cases will decrease in the following months. Salmonella infections, of which there were 48 cases in August, were reported in ten cases in September. Bacillary dysentery decreased from 53 in August to 11 in September, which is less than half the seven-year median. No cases of typhoid fever were reported.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Interior poliomyelitis was reported from Adams, 2, Arlington, 5, Ashfield, 1, Barnstable, 2, Belmont, 2, Boston, 40, Brockton, 1, Brookline, 2, Burlington, 1, Cambridge, 4, Canton, 3, Chelsea, 5, Chelsea Naval Hospital, 1, Dalton, 3, Dedham, 1, Falmouth, 1, Fitchburg, 1, Gardner, 1, Gloucester, 1, Haverhill, 1, Hinsdale, 1, Holliston, 1, Hull, 1, Lancaster, 1, Lawrence, 1, Leominster, 1, Lexington, 2, Lowell, 1, Lynn, 3, Lynnfield, 1, Malden, 6, Marblehead, 1, Medford, 3, Milton, 1, Nahant, 1, Newton, 2, North Adams, 4, Northampton, 4, Pittsfield, 9, Plymouth, 1, Princeton, 1, Quincy, 6, Reading, 1, Revere, 6, Richmond, 1, Rockport, 2, Salem, 3, Saugus, 1, Swansea, 1, Shrewsbury, 1, Springfield, 1, Wakefield, 1, Waltham, 4, Watertown, 1, Westboro, 1, Westwood, 3, Weymouth, 1, Winthrop, 2, Woburn, 1, Worcester, 2, total 163.
Diphtheria was reported from Boston, 3, Cambridge, 1, Chelsea Naval Hospital, 1, Foxboro, 1, Groton, 1, Melrose, 2, New Bedford, 1, Somerville, 1, Springfield, 1, Waltham, 2, total 14.

Dysentery, bacillary, was reported from Arlington, 1, Ayer, 1, Belmont, 2, Boston, 3, Cambridge, 1, Camp Edwards, 1, Hopkinton, 1, Malden, 1, total 11.
Encephalitis, infectious, was reported from Gardner, 1, total 1.
Hookworm was reported from Camp Edwards, 2, total 2.
Lymphocytic chorionmeningitis was reported from Ithurburg, 1, total 1.
Malaria was reported from Boston, 7, Cambridge, 1, Camp Edwards, 17, Danvers, 1, Fall River, 1, Fort Devens, 62, Haverhill, 1, Ipswich, 1, Melrose, 1, Millbury, 1, Orleans, 1, Quincy, 1, Waltham (regional hospital), 7, total 102.
Meningitis meningococcal was reported from Amesbury, 1, Chelsea, 1, Franklin, 1, Quincy, 1, total 4.
Meningitis, Pfeiffer bacillus, was reported from Springfield, 1, total 1.
Meningitis pneumococcal, was reported from Everett, 1, total 1.
Meningitis, other forms, was reported from Boston, 4, Everett, 1, total 5.
Meningitis undetermined was reported from Lenox, 1, total 1.
Salmonella infections were reported from Beverly, 2, Boston, 2, Cambridge, 2, Danvers, 1, Methuen, 1, Nahant, 1, Wakefield, 1, total 10.
Septic sore throat was reported from Attleboro, 1, Boston, 9, Cambridge, 2, Lynn, 1, Quincy, 1, Williamstown, 1, total, 15.
Tetanus was reported from Boston, 1, Medford, 1, total, 2.
Undulant fever was reported from Freetown, 1, Southbridge, 1, total 2.
Weil's disease was reported from Monson, 1, total, 1.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Lowell	November 2	Albert H. Brewster
Salem	November 3	Paul W. Hugenberger
Haverhill	November 7	William T. Green
Brockton	November 8	George W. Van Gorder
Worcester	November 16	John W. O'Meara
Pittsfield	November 19	Frank A. Slowick
Springfield	November 20	Garry deN. Hough, Jr.
Fall River	November 26	Eugene A. McCarthy
Hyannis	November 27	Paul I. Norton

MISCELLANY

SCHOOL-HEALTH PROGRAM

Because of the mutual interest of school administrators and administrators of public health, the Association of State and Territorial Health Officers adopted the following resolution at its annual meeting in Washington, D.C., on April 12, 1945:

This resolution divides the responsibility for school-health services between the two departments concerned. The primary responsibility for the educational aspects of health education are those of the school department. On the other hand, the prime responsibility for rendering services as given by the physician, nurse, dentist and others is that of the health department. Only by integrating the work of these departments, however, can this school-health program be a success, its ultimate goal being the achievement of optimal health on the part of all students, so as to enable them to profit the most from the opportunity offered them in the various schools and later to take advantage of any opportunity they may have to become successful and prosperous citizens.

It is the intention of the Association to support or oppose any legislation pertaining to school health according to the basic principle outlined in the resolution and the Association has invited the co-operation of all state superintendents of schools in this endeavor to achieve a better school-health program.

WHEREAS, School health programs in most communities are poorly organized, limited in scope and, in general, unproductive of better health, and

doubtedly the fact that he served for nine years as a member of the Board of Trustees of the Rockefeller Foundation was helpful to him in this regard. The founding and development of the Harvard School of Public Health was one of his great contributions. The tutorial system in the medical school and the general examinations were also started by him.

While he was dean, and definitely under his leadership, the Faculty of Medicine was strengthened by the appointment of many new professors, of whom a goodly proportion were brought from elsewhere, solely because of their apparent ability. During the tenure of his various posts, the Harvard Medical School not only increased in wealth but became national instead of local in its composition and outlook. The standards of scholarship, both among its students and among its faculty, were elevated. The contribution of the school to the acquisition of new medical knowledge was greatly extended.

His final period, that of his retirement, was divided between the mountains of North Carolina and Vermont, both of which he loved. A quiet life in the country was dear to his heart, but even so during this time he continued his good works, one of the last of which was that of serving as chairman of the Medical Advisory Committee of the Red Cross during the war just won.

The imprint of Edsall on medicine at Harvard, and beyond, is great. It will endure.

J H M

MASSACHUSETTS MEDICAL SOCIETY

EXECUTIVE COMMITTEE OF THE COUNCIL

On September 26, 1945, the Executive Committee of the Council, on the recommendation of the Committee on Membership and representatives from the supervising censors, took the following actions:

Allowed the following named fellows, applying for retirement and with all dues paid and in good standing, to retire under the provisions of Chapter I, Section 5, of the by-laws:

Bigelow, Edward B. (Worcester), 9 Walnut Street, Worcester
Cort, Parker M. (Hampden), Aetna Life Insurance Company, Hartford, Connecticut
Warren, Thomas F. (Bristol South), 341 Washington Street, Fall River

Allowed the following named fellows, applying for retirement, to retire with remission of dues owed the Society under the provisions of Chapter I, Section 5, of the by-laws:

Cogan, Edith I. (Essex South), 2 Broad Street, Salem
O'Sullivan, Anna (Suffolk), 370 Commonwealth Avenue, Boston
Ross, Elizabeth (nonresident), Shadyside Hospital, Pittsburgh, Pennsylvania
Shatswell, James A. (Essex South), 15 Thorndike Street, Beverly

Allowed the following named fellows, applying for resignation, to resign with remission of dues owed the Society, under the provisions of Chapter I, Sections 6 and 7 of the by-laws:

Berman, Nathaniel (Norfolk South), 1930 Wilshire Boulevard, Los Angeles, California
Kaye, Edward (nonresident), American Cyanamid Company, 30 Rockefeller Plaza, New York, New York.

Remitted the dues owed the Society of the following named fellow, who is a missionary, under the provisions of Chapter I, Section 6, of the by-laws:

Wilder, Edward W. (nonresident), Willard F. Pierce Memorial Hospital, Madura, South India

Reinstated the following named physician, under the provisions of Chapter I, Section 10, of the by-laws, who had been deprived of fellowship for the nonpayment of dues, provided his arrears in dues at the time of deprivation both to the Massachusetts Medical Society and to his district society, plus his dues for the year 1945 both to the Massachusetts Medical Society and to his district society be sent to the treasurer of the Society:

Rosenbloom, Carl W. (Hampden), 276 High Street, Holyoke

Allowed the following named fellows to change their membership from one district society to another, without change of legal residence, under the provisions of Chapter III, Section 3, of the by-laws:

Hall, John B., 17 Lane Park, Brighton 35 (office Roxbury) (remain in Norfolk)
Hamilton, Burton E., 30 Norfolk Road, Chestnut Hill (office Boston) (Norfolk to Suffolk)
Talbot, Nathan B., 10 Cottage Farm Road, Brookline (office Boston) (Norfolk to Suffolk)

Deprived the following named fellows of the privileges of fellowship, because of arrears of dues owed the Society, under the provisions of Chapter I, Section 8, of the by-laws:

Bloom, Robert R. (nonresident), Cedar Lane, Ossining, New York
Edelstein, Samuel (Norfolk), 31 Brookledge Street, Roxbury
Schroeder-Sloman, Sophie W. (nonresident), 750 South State Street, Elgin, Illinois
Zetlin, Arnold (nonresident), Shenandoah Avenue, Norfolk, Virginia

The personnel of the Committee on Membership is as follows: Harlan F. Newton, *chairman*, Roy V. Baketel, William A. R. Chapin, Peirce H. Leavitt, and Samuel N. Vose. The representatives of the supervising censors were as follows: William H. Allen, H. Quimby Gallupe, and Albert E. Parkhurst.

MICHAEL A. TIGHE, M.D., *Secretary*
Executive Committee

DEATHS

FAXON — Eudora W. Faxon, M.D., of Newton, died October 13. She was in her sixty-ninth year.

Dr. Faxon received her degree from Tufts College Medical School in 1904. She had conducted the Woodlawn Sanatorium for Epileptics, in West Newton for several years. She had also studied and practiced psychology at the University of Indiana, the Massachusetts State Hospital in Taunton, the Wrentham School for Feeble-Minded Children and the State Hospital for Women. She was a member of the New England Society of Psychology and the American Medical Psychological Society and a former member of the Massachusetts Medical Society.

HAYES — Capt. Paul Hayes, M.C., A.U.S., formerly of Milford, died October 1 in France of a gunshot wound. He was in his thirty-sixth year.

Dr. Hayes graduated from Bowdoin College and received his degree from Tufts College Medical School in 1935. After internship at the Worcester Memorial Hospital, the Maine General Hospital (Portland) and the State Hospital at Westfield, he settled in Milford, and at the time of enlisting in the

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NONTUBERCULOUS PNEUMONIA COMPLICATING PULMONARY TUBERCULOSIS

A Review of One Hundred and Eleven Cases*

GERALD F. HOGAN, M.D.†

PHILADELPHIA

FOR many years, certain clinicians have discussed the relation between pulmonary tuberculosis and pneumonia occurring in the same patient. Opinion has been unanimous concerning the low incidence of the combined diseases, but when explanations have been offered concerning the reasons for the low incidence, much diversity has appeared. There has been similar disagreement about the effect that either disease has on the other. In only a few cases have opinions been supported by case reports. This study was therefore undertaken in an attempt to answer the following questions: What is the incidence of these two diseases occurring in the same person? Are the course and outcome of the pneumonia altered by the presence of tuberculosis, whether active or inactive? Are the course and outcome of the tuberculosis altered by a superimposed pneumonia? Can any therapeutic inferences be drawn from this study?

REVIEW OF THE LITERATURE

Opinions in the literature concerning the relation between pneumonia and tuberculosis are few, and the reports of cases cited to substantiate such opinions are even fewer. Reports occurring prior to 1900—mostly in the German literature—were vitiated by inability to exclude the ever-present possibility of the pneumonia's being tuberculous. This handicap was overcome with the advent and use of the x-ray and more exact bacteriologic data. All agree that the incidence of the simultaneous presence of these diseases is significantly low. Baum and Amberson¹ quote Frankel as having observed 15 cases of pneumonia among 3250 tuberculous patients (0.46 per cent), and Schroder as having seen 2 cases in 6000 patients. Cecil² reports that pneumonia occurred in 2 patients out of 5000 at the Trudeau Sanatorium. Brock is quoted as having seen only 1 case of pneumonia and tubercu-

losis in thirteen years at Waverly Hills Sanatorium,³ and Heise,⁴ after thirty-five years of experience with sanatorium patients, has observed less than 6 such cases. Hayes⁵ states that among the tuberculous true lobar pneumonia is rare.

Similarly, in large series of pneumonia patients tuberculosis is rarely found. Frankel noted 15 such cases in 760 cases of pneumonia.⁶ Finland and his associates⁷ noted 33 cases of tuberculosis among 684 autopsies of patients dying of pneumococcal pneumonia. He⁸ further reports finding 29 patients with a positive sputum in a series of 3682 cases of pneumococcal pneumonia. Moore and his associates,⁹ grouping together pulmonary tuberculosis, recurrent pleurisy and pneumoconiosis, found only 24 such cases among 1469 pneumonia patients.

Few investigators have attempted to explain this low incidence. Calmett and Saenz¹⁰ found tuberculous guinea pigs especially resistant to inhalation infection with virulent pneumococci. Weissfeiler¹¹ explained this resistance on the basis of a nonspecific allergic reaction—the so-called "heteroallergic response." He was able to produce a typical Koch's phenomenon with organisms other than the tubercle bacillus, and by analogy he reasoned that likewise secondary invaders in a tuberculous patient set up a violent allergic response that destroys the invader before infection can be started.

Concerning the effect on the course and outcome of the pneumonia in this combination, there is a dearth of information. Bieling and Oelrichs¹² report that tuberculous rabbits react more vigorously to infection with pneumococci than do normal animals, but that the final outcome favors the tuberculous rabbits. Weissfeiler and others,¹³ trying to determine whether the course of the pneumonia is altered in rabbits with far-advanced tuberculosis, injected Type 1 pneumococci intraperitoneally and intravenously. The reaction in the tuberculous rabbits was slower and more exudative in type and tended more toward necrosis than in

*From the Department of Medicine and the Department of Tuberculosis, Philadelphia General Hospital.
†Formerly resident in medicine, Philadelphia General Hospital.

WHEREAS, There is a great confusion as to the division of responsibility between health and education departments for school-health programs and

WHEREAS, Adequate funds for the development of needed school-health programs are not available, and

WHEREAS, There is a serious lack of knowledge and technic by which school-health programs may be made a significant factor in improving the health of communities, and

WHEREAS, It is important that measures be taken to bring about the correction of remediable physical defects found among school children, and

WHEREAS, The school-health program is a significant factor in the child's learning process, thus accounting for the acquiring of erroneous concepts or ideas as a result of improper school-health programs, be it therefore

RESOLVED, That responsibility of school-health programs be recognized as a joint responsibility between the health and education departments on federal, state and local levels (In the development of improved school-health programs, joint committees of health and education departments should work out the details of the program together. In general, health education and physical education of school children should be regarded as a primary responsibility of the departments of education working in co-operation with, and with the assistance of, departments of health. Health and medical services rendered by physicians, dentists, nurses and other technical workers, including the followup in the home, constitute a responsibility of the health department, working in co-operation with and with the assistance of the department of education. In order that the educational program may be kept abreast of the most recent scientific and public-health knowledge, it is essential that health and education departments work together constantly on the content of school-health instruction) and be it further

RESOLVED, That appropriate federal agencies be requested to (1) carry out research and demonstrations to develop improved technics for school-health medical services and to evaluate existing technics, (2) carry out surveys to evaluate current practice in this field and to determine needs for expansion of services and (3) seek federal funds for the expansion of school-health programs in accordance with established needs, such funds to be allotted on a grant-in-aid basis to state health agencies

NOTICES

ANNOUNCEMENT

Dr. Donald E. Currier announces the opening of his office at 395 Commonwealth Avenue, Boston

NEW ENGLAND PATHOLOGICAL SOCIETY

A meeting of the New England Pathological Society will be held on Thursday, November 15, at 8 p.m., at the Mallory Institute of Pathology, Boston City Hospital. The entire program will be devoted to the subject of postwar education in pathology. Dr. Carl V. Weller, editor-in-chief of the *American Journal of Pathology*, and Dr. Frank W. Konzelmann, president of the American Society of Clinical Pathologists, will be the guest speakers.

Physicians and medical students are cordially invited to attend

HARVARD MEDICAL SOCIETY

A meeting of the Harvard Medical Society will be held in the amphitheater of the Peter Bent Brigham Hospital on Tuesday, November 13, at 8 15 p.m.

PROGRAM

Case presentation — Children's Hospital
Biochemical Studies on the Malarial Parasite Drs. E. G. Ball, C. B. Anfinsen, Q. M. Geiman and R. W. McKee
The Occurrence of Fibrinolysis in Shock Dr. Henry J. Tagnon
Pain in Men Wounded in Battle Dr. Henry K. Beecher

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9-10 a.m.

MEDICAL CONFERENCE PROGRAM

Friday, November 2 — Diagnosis and Radical Treatment of Intracranial Tumors Dr. William H. Sweet
Wednesday, November 7 — The Heart in Pregnancy Dr. Burton Hamilton
Friday, November 9 — Diuresis in Congestive Heart Failure Dr. Mark D. Altschule
Wednesday, November 14 — Tonsils and Aging Dr. C. W. Kelemen
Thursday, November 15 — Motion Sickness Dr. Robert L. Noble
Friday, November 16 — Deep Phlebitis and Pulmonary Embolus Dr. Jacob A. Fine
Wednesday, November 21 — Evolution of Industrial Medicine Dr. Dwight O'Hara
Friday, November 23 — Some Aspects of Penicillin Therapy Dr. Maxwell Finland
Wednesday, November 28 — Hypertension Dr. John C. Leonard
Friday, November 30 — The Use of Human Serum Albumin in the Treatment of Edema of Renal and Hepatic Origin Dr. George W. Thorn

On Tuesday and Thursday mornings Dr. S. J. Thannhauser will give medical clinics on hospital cases. On Saturday mornings clinics will be given by Dr. William Dameshek. All morning conferences are open to the medical profession.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, NOVEMBER 8

FRIDAY, NOVEMBER 9
*9:00-10:00 a.m. Medical clinic Isolation Amphitheater Children's Hospital
10:50 a.m. Postgraduate clinic in dermatology and syphilology Amphitheater, Dowling Building Boston City Hospital
12:00 m.-1:00 p.m. Clinicopathological conference (Boston Floating Hospital) Joseph H. Pratt Diagnostic Hospital
SATURDAY, NOVEMBER 10
*10:00 a.m.-12:00 m. Medical staff rounds Peter Bent Brigham Hospital
TUESDAY, NOVEMBER 13
*9:00-10:00 a.m. Medical clinic Infants' Hospital
*12:15-1:15 p.m. Clinicoroentgenological conference Peter Bent Brigham Hospital
WEDNESDAY, NOVEMBER 14
*12:00 m. Clinicopathological conference Children's Hospital
*7:15 p.m. Graduate seminar in pediatrics Children's Medical Service Amphitheater 3A, Massachusetts General Hospital

*Open to the medical profession

OCTOBER 1-DECEMBER 10, 1945 AND JANUARY 7-APRIL 22, 1946 Metropolitan State Hospital Eleventh postgraduate seminar in neurology and psychiatry Page 514 issue of September 6

NOVEMBER 2, 9 and 16 Salmon Lectures Page 514 issue of October 25
NOVEMBER 2-30 Joseph H. Pratt Diagnostic Hospital Medical conference program Notice above

NOVEMBER 7 Massachusetts Society of Examining Physicians Page 514 issue of October 25

NOVEMBER 8 *Fitfalls and Pleasures in the Treatment of Diabetes* Dr. Elliott P. Joslin Pentucket Association of Physicians 8:30 p.m. Haverhill

NOVEMBER 13 Harvard Medical Society Notice elsewhere on this page
NOVEMBER 15 New England Pathological Society Notice elsewhere on this page

NOVEMBER 17 Suffolk District Medical Society Page 514 issue of October 25

DECEMBER 13 Legislative Conference Page 514 issue of October 25

FEBRUARY 2 American Board of Obstetrics and Gynecology Page 514 issue of October 25

DISTRICT MEDICAL SOCIETIES SUFFOLK

NOVEMBER 17 Harvard Club of Boston

WORCESTER

NOVEMBER 14 Grafton State Hospital
DECEMBER 12 Worcester City Hospital
JANUARY 9 St. Vincent Hospital
FEBRUARY 13 Worcester State Hospital
MARCH 13 Worcester Memorial Hospital
APRIL 10 Hahnemann Hospital
MAY 8 Annual meeting

secondary patches of recent active tuberculosis. He concluded that the pneumonia reactivated the tuberculosis by a necrotizing process. In 1941, Pedigo and Coleman² reported a sanatorium patient with active tuberculosis who was treated with sulfonamides, with recovery from the pneumonia and no increase in the tuberculosis, and an ex-sanatorium patient with questionably active tuberculosis who was similarly treated with sulfonamides, with recovery and with doubtful activation, a cavity having been noted six weeks after the onset of pneumonia. A third patient was found at autopsy to have Type 3 pneumonia and a fibrocalcific tuberculous lesion in the same lobe, the latter showing no evidence of reactivation.

Finally, in 1942 was published the classic article of Baum and Amberson,¹ to which frequent reference has already been made. Appended to their paper is an extensive bibliography that covers many phases of nontuberculous pulmonary infections complicating pulmonary tuberculosis, not included within the scope of this paper.

ANALYSIS OF CASES

This section is concerned with a review of 111 cases of pneumonia complicating tuberculosis in 104 patients, 5 patients had more than one attack. These 111 cases constitute all the proved cases in which the patients were discharged from the Philadelphia General Hospital with the combined diagnoses, all of them between June, 1936, and June, 1944. Patients in whom one of the diseases was merely suspected were excluded from the study, as were all cases of tuberculous pneumonia. None of the patients were observed personally, all the data here presented having been assembled from the hospital records.

Almost all the roentgenograms were interpreted by one or the other of the two senior members of the Radiology Department, and the remainder by the resident radiologist. All the laboratory work was performed in the hospital laboratories by experienced personnel.

In this series there were 42 deaths, a mortality rate of 40 per cent, based on the number of patients. Autopsies were performed in 35 cases.

Pneumonia

The diagnosis of pneumonia was made on the basis of the history, physical findings and x-ray reports and the discovery of pneumococci in the blood or sputum. In the history, emphasis was placed on onset with chills, fever, pain on respiration, cough, a rusty sputum and dyspnea. Greater attention was paid to rigor and rusty sputum because of their rarity in tuberculous pneumonia and their frequent presence in pneumococcal lobar pneumonia. In addition to the finding on examination of evidence of infiltration or consolidation—

the lungs, special attention was paid to the presence of herpes labialis, which likewise has been found to be most unusual in tuberculous pneumonia.

In classifying the cases of pneumonia it was found that the terms "lobar pneumonia" and "bronchopneumonia" were insufficient because of their lack of specificity. To be sure, in discussing the relation between tuberculosis and pneumonia it is requisite to be as certain of the etiology of the pneumonia as of that of the tuberculosis. Hence, the pneumonia cases were divided into the following three groups in an effort to combine specificity with the x-ray and clinical classifications: Group 1 (45 cases), pneumococcal lobar pneumonia, Group 2 (23 cases), pneumococcal bronchopneumonia, and Group 3 (43 cases), bronchopneumonia of undetermined etiology.

In Group 1 there were 6 patients who had no adequate bacteriologic studies, but they are included because of the otherwise typical history, physical findings, x-ray appearances, response to treatment, typical resolution and so forth. In 3 of these patients, autopsy confirmed the diagnosis. The possibility of staphylococcal or streptococcal lobar pneumonia is recognized, but little significance can be attached to the erroneous inclusion of the rare case.

Group 3 in all probability contains many cases that would have been put in Group 2 if bacteriologic studies had been made, for in only 2 cases was this done, with a positive report for another organism (*Streptococcus haemolyticus*).

Table 1 summarizes the historical features of the complete series considered solely from the standpoint of the pneumonia. Attention is directed to the fact that the time between the onset of symptoms and admission to the hospital was much longer in Group 3 than in the two other groups, and to the symptoms in all groups, which in order of frequency were cough, fever, pain, dyspnea, chills, a rusty sputum and herpes labialis. The last occurred only in the cases of pneumococcal pneumonia. Great discrepancy is likewise noted between the incidence of chills in Group 1 as compared with Groups 2 and 3.

In regard to the number of symptoms per patient, pneumonia was considered the likeliest diagnosis on the basis of the history alone if four or more symptoms were present. This was so in 51 per cent of the patients in all these groups.

Table 2 summarizes some of the physical findings, including involvement as determined by physical and x-ray examination.

Table 3 summarizes the important laboratory data, and Table 4 the treatment directed toward the pneumonia and the outcome. The high percentage of deaths in the total series (38 per cent) is due to the moribund condition of some patients on admission, as well as to the occurrence of pneumonia before the advent of the sulfonamides.

normal animals, and in response to the added infection a proportionately larger role was played by the reticuloendothelial system. Finland and his co-workers⁷ state that the pneumonia associated with tuberculosis is likely to be bronchopneumonic in character and to be caused by a pneumococcus of Type 3, 8, 10, 18 or 20. In another report, he⁸ concludes that pneumococcal bronchopneumonia is usually a secondary complication of other serious disease, and hence has a higher mortality rate than do other types. Moore et al.¹⁴ believe that tuberculosis lowers the resistance to pneumococcal infection and that its presence increases the complication rate.

The effect of intercurrent pulmonary infections on the tuberculous process has been studied somewhat more thoroughly. Thus during the pandemic of influenza in 1918-1919 several reports appeared in the literature showing that activation of the tuberculosis took place in as many as 50 per cent of some series.¹⁵⁻¹⁷ Similarly, many authors have been concerned with the activation that occurs with lung abscesses and purulent lung infections.¹⁸ When one comes to pneumonia, however, the only extensive investigation was conducted by Baum and Amberson.¹ They presented a series of 102 cases of pneumonia in 97 tuberculous patients. Because of the size of this group, they concluded that pneumonia was not rare in the tuberculous population, although they do not state the incidence that they observed. They believe that pneumonia has potentialities for causing activation of a tuberculous lesion, for in their series definite activation was caused in 8 cases, probable activation in 10 and doubtful activation in 11. Sixty-five cases showed no activation.

The attempt to explain the pathogenesis of reactivation brings forth several possibilities. Krause¹⁹ believes that the inflammation with its attendant congestion puts such a strain on the fibrous capsule that surrounds the tuberculous nodule that this capsule is gradually destroyed, resulting in the liberation of the tubercle bacilli. Pagel²⁰ explains it on the basis of heteroallergy, and shows that liquefaction is a result of this allergic response—a response that can be set up by secondary invaders like the pneumococcus.

Perhaps the most important factor, however, is the destruction of the capsule by pulmonary supuration. This point is well taken by Baum and Amberson,¹ who observed a high incidence of activation in cases of bronchiectasis and in lung abscesses. Destruction by a putrid necrosis likewise can set the bacilli free. Kessel²¹ has adequately described this type of pulmonary parenchymal necrosis as occurring in areas of resolving pneumonia. He attributes the destruction to thrombosis of the artery supplying the area involved, with ensuing infarction and formation of an aputrid abscess. Because these areas frequently do not open to a

bronchus, the abscess remains uncontaminated by pyogenic organisms. He holds that thromboses of tiny end arteries are frequent and that the small cavities produced, although not of sufficient size to give evidence of their presence, may easily result in autolysis of the fibrous tuberculous capsule. These areas of necrosis have been commented on by other authors as well.²²⁻²⁴

Baum and Amberson¹ conclude as follows:

We believe that the reason for the failure of pneumonia to activate the majority of tuberculosis cases lies in the site of attack by the most frequent infecting organism—the pneumococcus. This organism is primarily an alveolar pathogen and interstitial invasion is the exception rather than the rule, conspicuous only in Type 3. Suppuration within the pneumonic area is the most important factor in subsequent activation of a tuberculous lesion.

In regard to Type 3, all those who have dealt with large series of cases have recognized the unusual invasive features of Type 3 pneumonia.^{7,8,25}

Poindexter²⁶ has furnished evidence that the presence of secondary organisms heightens the virulence of the tubercle bacillus. McPhedran,²⁷ at the other extreme, has presented a series of 51 cases of tuberculosis, one third of which were probably inactive, in each of which the development of a nonspecific parenchymal infection in one or both paracardiac areas was followed by regression of the tuberculous lesion in one of the upper lobes. In another communication, however, he²⁸ reports 4 cases, among others, in which a bronchopneumonia caused miliary spread of tuberculosis by "flooding" the nodes rather than by depressing resistance. He²⁹ maintains:

The chief effect on pre-existent tuberculous lesions of acute pulmonary respiratory disease is probably a quasi-mechanical one, whereby the lymph drainage, increased by the acute infection, sweeps into the circulation tubercle bacilli from the already extensively damaged lymph node.

Five papers have been discovered in the English literature that present case reports. In 1937, Pagel³⁰ reported a case of pneumonia occurring in a patient with quiescent tuberculosis, and offered the first definite histologic proof of liquefaction and liberation of the tubercle bacilli by the pneumonic process. In 1939, Crawford³¹ presented a case of fibrocavicular and cavernous tuberculosis in the right upper lobe and right midzone, with mottling in the entire left lung and a cavity in the left upper lobe. A pneumonic consolidation occurred in the right lower lobe, and the sputum was found to contain both Type 1 pneumococcus and tubercle bacilli. The patient developed a Type 1 empyema, was treated with sulfanilamide and recovered with no increase in the tuberculosis. In 1940, Moolten,³² reporting a case of pancreatic lithiasis, called attention to the findings of a pneumonia in the right upper lobe previously involved in a tuberculous process. He described the histologic picture of destruction of the envelope of scar tissue around the tubercle with release of caseous contents and the adjacent

Treatment of the tuberculosis, when it was discovered, was given according to the usual procedure followed in the Division of Tuberculosis — bed rest with supplementary treatment when indicated

PNEUMONIA AND TUBERCULOSIS COMBINED

The foregoing sections have analyzed this series as composed of some patients with pneumonia of one sort or another, and of others with pulmonary

TABLE 5 Activity of Tuberculosis in the Pneumonia Groups

	PNEUMOCOCCAL LOBAR PNEUMONIA	PNEUMOCOCCAL BRONCHO- PNEUMONIA	BRONCHO- PNEUMONIA OF UNDETERMINED ETIOLOGY	TOTALS
Active	16	2	14	32 (29%)
Inactive	29	21	29	79 (71%)
Totals	45	23	43	111

tuberculosis in some stage of activity or healing. The series will now be considered from the viewpoint of the two diseases combined. The incidence of the combination, as in the reports of other investigators, was low. During the period covered by this

The course was considered typical if there was crisis or lysis of the fever, clinical improvement and recovery and no sequelae, such as empyema, recurrent fever and so forth. The reverse of these criteria constituted an atypical course, and these patients naturally included all those who died during the pneumonia. Since 60 of these patients were treated specifically (Table 4), it is desirable to know whether the course was altered in the treated group as compared with the untreated group in relation to the degree of activity of the tuberculosis. Table 6 summarizes the data on this point.

It will be seen that the course of the pneumonia was atypical in 23 (72 per cent) of the 32 cases with active tuberculosis and in 43 (54 per cent) of the 79 cases with healed or inactive tuberculosis. There are so many other variables that it is impossible to ascribe this difference solely to the presence of tuberculosis in active form, but it seems reasonable to conclude that the course of the pneumonia is likelier to be altered if the tuberculosis is active than if it is healed or quiescent.

Again, of the 14 active cases that received specific

TABLE 6 Course of Pneumonia in Relation to Specific Treatment and Activity of Tuberculosis

TYPE OF TUBER- CULOSIS	PNEUMOCOCCAL LOBAR PNEUMONIA				PNEUMOCOCCAL BRONCHO- PNEUMONIA				BRONCHOPNEUMONIA OF UNDE- TERMINED ETIOLOGY				TOTALS
	TYPICAL		ATYPICAL		TYPICAL		ATYPICAL		TYPICAL		ATYPICAL		
	Specific Treatment	Non- specific Treatment	Specific Treatment	Non- specific Treatment	Specific Treatment	Non- specific Treatment	Specific Treatment	Non- specific Treatment	Specific Treatment	Non- specific Treatment	Specific Treatment	Non- specific Treatment	
Active	4	0	9	3	0	1	0	1	0	4	1	9	32 (29%)
Inactive	11	3	12	3	6	4	9	2	8	4	2	15	79 (71%)
Totals	15	3	21	6	6	5	9	3	8	8	3	24	111

study, there were 6737 cases diagnosed as pneumonia, the incidence of tuberculosis among which was 16 per cent. During the same period there were 8487 patients with tuberculosis. Hence, the incidence of pneumonia among the tuberculous patients was 13 per cent, and the incidence of the combination among the total patients with tuberculosis or pneumonia was 0.73 per cent. Regardless of how one calculates the incidence, the fact that these two extremely prevalent diseases occur in combination in such a low incidence is startling. Obviously this requires explanation. Some opinions on this question were quoted above in the review of the literature, further brief comment on this point will be made in the discussion.

The next question is the effect that tuberculosis has on the course and outcome of pneumonia. When this series is compared with large series of uncomplicated cases of pneumonia, it is seen that the onset and clinical manifestations approximate closely, but this is not true as concerns the course and outcome.

Course

The cases have been grouped as those with a typical course and those with an atypical one.

treatment 10 (71 per cent) ran an atypical course, whereas of the 18 that received no specific treatment 13 (72 per cent) did so. Of the 48 inactive cases that received specific therapy 23 (48 per cent) ran an atypical course, and of the 29 that received no specific treatment 20 (69 per cent) did so. Hence, it seems that the number of tuberculous patients with pneumonia who run an atypical course is not altered to any great degree by the specific therapy of the pneumonia, except in those with inactive tuberculosis. This is not to say, however, that the sulfonamides did not modify the clinical course of pneumonia in certain cases. Furthermore, this is perhaps an unfair judgment of the efficacy of the sulfonamides, since in many of the patients death probably occurred before adequate blood levels of the drug had been obtained.

Outcome

The effect of tuberculosis on the outcome of pneumonia is shown in Table 7. Among the 32 active cases, death occurred in 18 (56 per cent), and among the 79 inactive cases it occurred in 24 (30 per cent). Thus, the deaths were twice as numerous when the tuberculosis was active than when it was inactive.

Tuberculosis

Tuberculosis was known to have existed in 40 of the 111 cases. Thirty-four of these patients had been under treatment at a hospital at one time or

TABLE 1 Historical Features of 111 Cases of Simultaneous Pneumonia and Tuberculosis, Considered from the Standpoint of the Pneumonia

HISTORICAL FEATURE	PNEUMOCOCCAL LOBAR PNEUMONIA	PNEUMOCOCCAL BRONCHO-PNEUMONIA	BRONCHO-PNEUMONIA OF UNDETERMINED ETIOLOGY	TOTALS
Age				
0-9 yr	0	1	1	2
10-19 yr	0	1	3	4
20-29 yr	4	0	1	5
30-39 yr	11	3	5	19
40-49 yr	11	6	5	22
50-59 yr	11	5	10	26
60-69 yr	6	2	13	21
70 yr	2	5	5	12
Sex				
Male	30	18	29	77
Female	15	5	14	34
Color				
White	28	17	31	76
Negro	17	6	12	35
Time from onset to admission				
1 day	4	5	4	13
2 days	3	0	1	4
3 days	5	3	2	10
4 days	7	2	3	12
5 days	5	0	2	7
6 days	6	4	1	11
7 days	2	3	4	9
8 days	1	1	1	3
9 days	2	0	0	2
10 days	5	1	1	7
11 days	2	4	13	19
Unknown	3	0	11	14
Major symptoms				
Cough	42 (96%)	22 (95%)	40 (93%)	104 (94%)
Fever	44 (98%)	22 (95%)	35 (81%)	101 (90%)
Pain	32 (72%)	16 (69%)	20 (46%)	68 (61%)
Dyspnea	31 (70%)	8 (35%)	26 (60%)	65 (59%)
Chills	29 (64%)	9 (39%)	13 (30%)	51 (46%)
R. sput.	16 (36%)	7 (30%)	6 (14%)	29 (26%)
Herpes	5 (11%)	1 (4%)	0	6 (5%)
Number of symptoms per patient				
1	0	0	2	2
2	4	4	10	18
3	6	8	10	24
4	12	5	16	33
5	13 (78%)	3 (48%)	5 (49%)	21 (51%)
6 or 7	10	3	0	13

another, and 6 were under treatment at the time of the development of pneumonia. There were in addition 14 patients with a decidedly typical history

TABLE 2 Case Incidence of Clinical and Roentgenographic Findings

FINDING	PNEUMOCOCCAL LOBAR PNEUMONIA	PNEUMOCOCCAL BRONCHO-PNEUMONIA	BRONCHO-PNEUMONIA OF UNDETERMINED ETIOLOGY	TOTALS
Temperature on admission				
99 or lower	3	2	13	18
100	4	3	7	14
101	6	4	8	18
102	12	4	4	15
103	7	4	3	18
104 or higher	13	2	3	18
Number of lobes involved				
1	28	13	23	64
2	15	7	10	32
3 or more	2	3	10	15
Frequency of significant disease other than tuberculosis	26	9	19	54 (50%)

and repeated close contact with open tuberculosis at home, who were consequently considered to have the disease on admission. Hence, there were 54 patients in whom tuberculosis was, with relative certainty, known to be present at the onset of pneumonia. In the remaining 57 cases, the tuber-

culosis was diagnosed after admission, mainly on the basis of x-ray evidence or the presence of tubercle bacilli in the sputum. In fact, most of the patients

TABLE 3 Case Incidence of Significant Important Laboratory Findings

	PNEUMOCOCCAL LOBAR PNEUMONIA	PNEUMOCOCCAL BRONCHO-PNEUMONIA	BRONCHO-PNEUMONIA OF UNDETERMINED ETIOLOGY	TOTALS
Maximum white-cell count (in thousands)				
5-9	2	4	4	10
10-14	6	4	2	12
15-19	10	3	3	16
20-24	6	4	1	11
25-29	8	2	2	12
30 or over	7	1	2	10
Percentage of neutrophils in total white-cell count				
40-49	1	0	0	1
50-59	0	1	1	2
60-69	0	0	5	5
70-79	4	2	1	7
80-89	13	12	4	29
90-100	21	4	4	29
Blood culture				
Positive	10	1	0	11
Negative	23	7	4	34
Organisms in sputum or blood, or both				
Pneumococcus				
Type 1	4	1	—	5
Type 2	2	0	—	2
Type 3	4	0	—	4
Type 4	4	2	—	6
Type 5	1	1	—	2
Type 6	1	0	—	1
Type 7	3	1	—	4
Type 8	3	0	—	3
Type 13	0	1	—	1
Type 16	1	0	—	1
Type 17	1	1	—	2
Type 20	2	0	—	2
Type 22	1	0	—	1
Type 25	1	0	—	1
Untyped	8	15	—	23
Secondary to pneumococcus	10	8	—	18
Other than pneumococcus	2	—	2	4
Not examined	7	—	41	48

came to the hospital because of the pneumonia. Only 35 were either admitted to the tuberculosis wards or were already on those wards when pneumonia developed. The rest were sent to the Fever Ward — a special ward for pneumonia patients.

The tuberculosis was classified as active (32 cases) and inactive (79 cases) (Table 5). The disease was considered to be active if it was known to have been so shortly before the onset of the pneumonia,

TABLE 4 Treatment Directed toward Pneumonia, and Outcome

TYPE OF TREATMENT	PNEUMOCOCCAL LOBAR PNEUMONIA		PNEUMOCOCCAL BRONCHO-PNEUMONIA		BRONCHO-PNEUMONIA OF UNDETERMINED ETIOLOGY		TOTALS	
	LIVING	DEAD	LIVING	DEAD	LIVING	DEAD	LIVING	DEAD
Sulfonamides	20	8	10	2	8	2	38	12
Antipneumococcus serum	1	0	0	0	0	0	1	0
Sulfonamides and serum	4	2	1	0	0	0	5	2
Supportive treatment	8	1	6	4	11	16	25	21
No treatment	0	1	0	0	0	6	0	7
Totals	33	12	17	6	19	24	69	42

or if there was a positive sputum or x-ray evidence of cavitation or soft, exudative lesions that showed marked changes from one film to the next. Otherwise it was considered to be inactive.

DISCUSSION

The preceding section has given a statistical analysis of these cases. To obtain a clearer picture of the situation, certain points need comment. Thus, the extremely low incidence of the combina-

TABLE 10 *Topographical Relation between Pneumonia and Tuberculosis*

LOCATION OF PNEUMONIA	REACTIVATION OF TUBERCULOSIS			TOTALS
	DEFINITE OR DOUBTFUL UNKNOWN PROBABLE	OR NONE		
Pneumonia in tuberculous lobe	3	38	5	46 (41%)
Pneumonia not in tuberculous lobe	1	54	10	65 (59%)
Totals	4	92	15	111

tion of pneumonia and tuberculosis has been noted. The fact that these diseases occur together is beyond dispute. One should note, however, that the tuberculosis was active in only 29 per cent of the series, and that in little less than half of these the pneumonia was a terminal event. Hence, one rarely finds a tuberculous patient with active disease who develops pneumonia and recovers from it and continues to have active tuberculosis. According to the records of the Philadelphia General Hospital, with 2700 beds, it occurred in only 14 cases in eight years. Baum and Amberson¹ are inclined to attribute this extraordinarily low incidence in part to the sheltered life of sanatorium patients, but this institution is a city hospital with chiefly charity beds, and its patients in the main lead quite the reverse of sheltered lives.

Is there some antithesis between the growth characteristics of the pneumococcus and those of the tubercle bacillus such as to prevent their simultaneous growth? This is a question to which there is at present no adequate answer. The views of others, quoted above, present explanations that are not completely satisfactory.

CONCLUSIONS

From this study the following conclusions may be drawn. First, the incidence of pneumonia complicating pulmonary tuberculosis is significantly low. The occurrence of nonterminal pneumonia in a patient with active tuberculosis is extremely infrequent, less than 2 cases a year being observed at the Philadelphia General Hospital. Second, the course of pneumonia is altered by the presence of tuberculosis. Of this series of 111 cases, 60 per cent ran an atypical course — 72 per cent of the active cases and 54 per cent of the inactive ones. Third, the outcome of pneumonia is altered by the presence of tuberculosis. In this series the death rate was 38 per cent, but the deaths were almost twice as numerous when the tuberculosis was active (56 per cent) as when it was inactive (30 per cent). Fourth, reactivation of a tuberculous focus that is quiescent or an increase of disease in already active

tuberculosis may be expected in 15 per cent of the patients who develop superimposed pneumonia, whether or not it is in the same lobe and whether or not it is specifically treated. Lastly, no definite therapeutic implications have been derived from this study. The question of bacterial antagonism was not a subject of this paper, but if this is the correct explanation of the infrequency of pneumonia complicating tuberculosis, therapeutic use of the products of the pneumococcus might well be made in the treatment of pulmonary tuberculosis. This appears to be a fertile field for future investigation.

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It is now to be determined whether tuberculosis is altered by superimposed pneumonia. To this end, the series has been regrouped according to whether the tuberculosis was activated and to

that persisted four or more weeks after the onset of pneumonia. Since more and more cases of slowly resolving pneumonia are coming into the reported series, it is quite probable that some of these, es-

TABLE 7 Outcome of Pneumonia in Relation to Type of Therapy and Activity of Tuberculosis

TYPE OF TUBERCULOSIS	PNEUMOCOCCAL LOBAR PNEUMONIA		PNEUMOCOCCAL BRONCHOPNEUMONIA		BRONCHOPNEUMONIA OF UNDETERMINED ETIOLOGY		TOTALS
	SPECIFIC TREATMENT	NONSPECIFIC TREATMENT	SPECIFIC TREATMENT	NONSPECIFIC TREATMENT	SPECIFIC TREATMENT	NONSPECIFIC TREATMENT	
Active							
Alive	6	3	0	1	0	4	14
Dead	6	1	0	1	1	9	18
Inactive							
Alive	18	6	11	5	8	7	55
Dead	4	1	2	3	1	13	24
Totals	34	11	13	10	10	33	111

what degree — that is, definite activation, probable activation, doubtful activation, no activation and activation unknown. In so doing, the criteria of Baum and Amberson have been employed. They state

Definite activation was thought to have taken place when there was post-mortem evidence of recent activation or when, following pneumonia, pulmonary tuberculosis, which previously had been stationary or latent, became progressive.

To the category of probable activation were assigned cases in which previously inactive pulmonary tuberculosis showed signs of activity, though not of progression, there was spread of previously active tuberculosis coinciding with the pneumonia, and early death was due apparently to progressive tuberculosis, although post-mortem examination was lacking.

The category of doubtful activation included cases of tuberculosis showing temporarily a positive sputum during the course of pneumonia, cases showing residual areas of density in the roentgenogram, in which differentiation between spread of tuberculosis and postpneumonic pulmonary fibrosis was not possible, and cases showing progression of tuberculosis later than one month but sooner than one year after subsidence of the pneumonia.

No activation was considered to have taken place when there was no change in the tuberculous lesion or its activity, or when progression of the tuberculosis occurred later than one year after subsidence of pneumonia, the latter having left behind no suppurative lung disease.

The degree of activation was considered to be unknown when death occurred too soon to show an effect clinically and when no post-mortem examination was done. It was also considered unknown when no adequate information was at hand regarding the status of tuberculosis at the time the pneumonia took place, even though there was progressive tuberculosis following the pneumonia.

Table 8 shows the number of cases in each category in relation to the pneumonia. The rather

TABLE 8 Type of Activation according to Type of Pneumonia

TYPE OF ACTIVATION	PNEUMOCOCCAL LOBAR PNEUMONIA	PNEUMOCOCCAL BRONCHOPNEUMONIA	BRONCHOPNEUMONIA OF UNDETERMINED ETIOLOGY	TOTALS
Definite	2	1	0	3
Probable	1	0	0	1
Doubtful	5	5	5	15
None	28	14	34	76 (68%)
Unknown	9	3	4	16
Totals	45	23	43	111

large number of patients in the doubtful group were placed there mainly because of residual shadows

especially those in Group 3, were virus or other slowly resolving types of pneumonia, and that if more accurate diagnostic facilities had been available they would have been grouped with those that showed no reactivation.

In the unknown group, several showed progressive disease, but they were so placed because the prepneumonic status of the tuberculosis could not be determined. It was similarly probable that some of these rightfully belong in the group with definite activation.

Table 9 shows the occurrence of reactivation in relation to the type of tissue reaction of the tuberculosis. It is considered that definite, probable or

TABLE 9 Reactivation of Different Pathologic Types of Tuberculosis

TYPE OF TISSUE REACTION	TYPE OF REACTIVATION					TOTALS
	DEFINITE	PROBABLE	DOUBTFUL	NONE	UNKNOWN	
Predominately exudative	1	0	2	5	4	12
Predominately fibro-productive	0	0	8	25	1	34
Fibrocavernous	1	1	1	12	4	19
Fibroid and calcific	1	0	4	32	3	40
Under collapse therapy	0	0	0	2	0	2
Totals	3	1	15	76	16	111

even doubtful reactivation is a serious alteration of the disease. Furthermore, in most cases this reactivation, despite other variables, was probably due to superimposed pneumonia.

Table 10 shows the topographic relation of pneumonia and tuberculosis. In 46 cases in the series (41 per cent), at least one lobe was involved by both diseases. Each case was counted once even though more than one lobe was involved in either process. The remaining 59 per cent had pneumonia in a lobe or lobes that were not involved by tuberculosis. It is seen that 83 per cent of the total fall into the group of doubtful or no activation. This permits the conclusion that superimposed tuberculosis is likely to give rise to reactivation of tuberculosis in approximately 15 per cent of cases.

the left lung, with several small cavities in the 1st and 2nd interspaces. Twelve days later, another chest film disclosed some increase of disease in the left lung with cavitation present in both the left upper and left lower lobes. After the first x-ray report sputum studies were undertaken but a positive sputum was not obtained until 6 months after admission. Subsequently, the patient went downhill, the disease spread to the opposite lung, and she died of widespread tuberculosis.

Comment Because of her history of frequent colds with expectoration of blood, it may be assumed that this patient had active pulmonary tuberculosis. A multilobar invasion with the pneumococcus resulted, in all probability, in the rapid spread of the tuberculosis in the lobes that were involved in the superimposed inflammation. Although this is probably one of the most definite cases of active tuberculosis with superimposed lobar pneumonia yet encountered, because of the lack of knowledge of the status of the tuberculosis at onset it is classified as probable reactivation. It is of interest that this patient was one of the 9 who had active tuberculosis with a superimposed pneumococcal lobar pneumonia but did not die during the pneumonia—that is, from the combination of the two diseases.

CASE 6 (No 74913) The patient, a 29-year-old man, was admitted with a history of known pulmonary tuberculosis for 13 years, many of which were spent at a sanatorium. He was at home awaiting a call to return to the hospital for a left thoracoplasty for upper lobe disease. Two weeks before admission he had a sudden onset of chills, fever, pain around the left lower chest, increased by deep inspiration, and an increase in coughing and expectoration.

Physical signs on admission were those of atelectasis of the left upper lobe and consolidation of the left lower lobe. These findings were confirmed by x-ray examination, which in addition demonstrated healed disease in the right upper and middle lobes. A Type 17 pneumococcus was abundant in the sputum.

The course during the first week or so was stormy, with extreme dyspnea, cyanosis and a temperature that fluctuated between 100 and 102°F. On the 7th day, the administration of sulfathiazole was begun, and the patient gradually improved. Two weeks after admission when he was clinically improved, the sputum was found to be positive for tubercle bacilli.

Three weeks after admission there was a relapse, with dyspnea, cyanosis and a temperature of 103°F. X-ray examination disclosed atelectasis of the left upper lobe and effusion at the left base. The chest was tapped, with removal of purulent fluid, culture of which revealed pneumococci but no tubercle bacilli. At that time the sputum still showed abundant Type 17 pneumococci. The patient received a course of sulfapyridine and within a few days seemed to be convalescing normally. Two weeks later he had a second relapse, with dyspnea, cyanosis and fever. Fluoroscopy demonstrated atelectasis of the left upper lobe, mottled density of the left lower lobe and scattered densities in the right lung. The next day the patient was found dead in bed.

Post-mortem examination showed fibrosis, atelectasis and encapsulated caseous tuberculosis with activation in the left lung, and nontuberculous bronchopneumonia in the right lung.

Comment This case was one of long-standing pulmonary tuberculosis, which had become sufficiently stationary for a thoracoplasty to be planned. It appears that the lobar pneumonia was the starting point of the downward course. The case is unusual in that the patient not only developed lobar pneumonia but had a relapse with pneumococcal empyema and then a terminal bronchopneumonia, presumably due to the same organism. In view of the autopsy findings this case is classified as one of definite reactivation.

CASE 7 (No 56302) The patient, a 30-year-old woman, was known to have had tuberculosis for 12 years. The main lesions were in the right upper lobe. Five months prior to admission, check-up films revealed progression of the lesions. On the day before admission the patient developed a sudden pain in the left chest, fever, shortness of breath and an increase in cough and slight hemoptysis.

On admission, the temperature was 104°F, the pulse 150, and the respirations 50. Rales were heard throughout the chest, but there was evidence of consolidation of the left lower lobe. The patient was acutely ill and was placed in an oxygen tent and treated with sulfathiazole. The white-cell count was 10,600, with 92 per cent polymorphonuclear leukocytes. The sputum contained Type 2 pneumococci but no tubercle bacilli were found. The course in the hospital was extremely hectic, and despite treatment death occurred 3 days after admission.

Autopsy disclosed typical lobar pneumonia in the left lower lobe, and caseous tuberculosis with cavitation in the right upper lobe.

Comment This case was one of lobar pneumonia developing in a patient with active progressing tuberculosis confirmed by autopsy. The cause of death was attributed equally to the pneumonia and to the tuberculosis. There was no reason to believe that the pneumonia caused any increase in the activity of the tuberculosis, especially since the patient did not live long enough to show whatever increase may have taken place. Hence this case is placed in the no-reactivation group.

CASE 8 (No 123077) The patient, a 52-year-old man, entered the hospital with a 4-day history of acute illness. He had been working and well, except for a chronic cough, when he suddenly developed a chill, fever, chest pain and an increase in the cough, with production of thick, non-bloody sputum.

On admission the temperature was 102°F, the pulse 118, and the respirations 28. There was evidence of scattered patches of consolidation in both lower lobes.

Treatment with sulfathiazole was begun, and within 2 days the temperature was normal remaining so. The lung fields began to clear. An x-ray film taken on the 7th hospital day—11 days after the onset—showed fibrous strands and pleural thickening in each apex due to minimal healed tuberculosis, and haziness in the right base, due to recent pneumonia. The sputum was negative for tubercle bacilli. The patient had an uneventful convalescence and was discharged well after being hospitalized for 14 days. He remained well, although with some continued weight loss, for 6 months, at which time the cough and expectoration of greenish sputum increased. Three months later he was readmitted for these complaints. At this time he was found to have a positive sputum, and x-ray examination showed mottling and fibrosis of the entire right upper lobe, several small cavities in the 2nd interspace and bronchogenic spread to the midportion of the left lung. The patient continued to regress and died of widespread tuberculosis 5 months after the second admission.

Comment This is a case of pneumonia developing in a person with apparently healed tuberculosis. Because the tuberculosis became reactivated between 6 and 9 months after the episode of pneumonia, the case is considered one of doubtful reactivation. Presumably, the lesion in the right upper lobe broke down and started the final illness. It is interesting to observe that the pneumonia was in the lower lobes and the tuberculosis in the upper, a fact that casts a little further doubt on the role of the pneumonia in the pathogenesis of reactivation.

CASE 9 (No 143818) The patient, a 38-year-old Negro, was well until 6 days before admission when he developed a "cold." Soon afterward he had a chill, followed by chest pain, fever and cough productive of blood-tinged sputum.

On examination the temperature was 100°F, the pulse 120 and the respirations 35. There was evidence of consolidation of the right upper and middle lobes. Admission cultures of the throat and sputum were replete with pneumococci, but a blood culture was negative. The white-cell count was 19,400, with 84 per cent polymorphonuclear leukocytes. The patient was treated with sulfamerazine, and within 36 hours the temperature returned to normal, remaining so. On the 4th hospital day, x-ray examination revealed consolidation of the right upper and middle lobes. On the 7th day a smear of the sputum was found to be positive for tubercle bacilli and the patient was transferred to the Tuberculosis Division. Subsequent to this there were positive sputums on the 30th, 38th and 50th days. Between these dates there were six negative sputums.

CASE REPORTS

CASE 1 (No 127446) The patient, a 56-year-old Negress, was apparently in usual health until 2 weeks before admission, when she developed a "cold." Not long afterward she had chills and fever, became short of breath and noted pain in the right lower chest, aggravated by inspiration and coughing. These symptoms were severe during the 3 days prior to admission. There was no hemoptysis and no history of previous respiratory disease.

On admission the patient was acutely ill, mildly confused and markedly dyspneic. The temperature was 103°F, the pulse 120, and the respirations 60. Coarse rales were heard throughout the lung fields, but there was definite evidence of consolidation of the right lower lobe. Treatment was started with sulfamerazine, but because of the patient's serious condition she was placed in an oxygen tent. Despite all efforts she died within 12 hours of admission.

Autopsy disclosed a typical lobar pneumonia of the right lower lobe, bronchopneumonia of the left lower lobe and fibroexudative tuberculosis of the left upper lobe, with recent tuberculosis of the right upper lobe. Histologically the pneumonia was shown to be nontuberculous.

Comment This patient was found to have active tuberculosis with active pulmonary inflammation, probably pneumococcal in origin. The fact that she was apparently well until approximately 2 weeks before admission indicates that the tuberculosis found in the right upper lobe was a recent spread from a newly activated focus in what was probably an area of quiescent tuberculosis, the reactivation occurring in the course of the secondary infection of the lung. It is of interest that the lobe that was consolidated was not the one that harbored the original tuberculous infection. This case is classified as one of definite reactivation.

CASE 2 (No 94071) The patient, a 68-year-old Negro, was admitted in a feeble condition. The history was incomplete, but he had been sick for 4 weeks with a non-productive cough, weight loss, night sweats and indefinite chest pain.

On admission, the temperature was 101°F. There was jaundice, and evidence of consolidation was found over the left upper and right middle lobes. A diagnosis of bilateral pulmonary tuberculosis was made. A throat culture grew pneumococci, and a blood culture made on admission grew Type 8 pneumococci. The icteric index was 48. X-ray examination of the chest showed consolidation of the right upper and middle lobes and the left upper lobe.

The patient was treated with sulfadiazine, with only a fair response. Six days after admission, he developed consolidation of the left lower lobe. A repeat blood culture was negative. He grew weaker and died.

Autopsy showed pneumococcal lobar pneumonia involving the right upper and the left lower lobes, with marked organization, together with bilateral chronic apical tuberculous cavitation. The patient was also suffering from lymphoid leukemia, which was discovered in the histologic sections.

Comment This patient had a proved active lobar pneumococcal pneumonia with pneumococcemia and simultaneously active cavernous tuberculosis. One of the tuberculous lobes was also involved in the process of lobar consolidation. Yet no evidence of reactivation was demonstrable, and death was ascribed to the pneumonia.

CASE 3 (No 89869) The patient, a 41-year-old Negress, was admitted in a critical condition. For several months she had had a chronic cough and night sweats, together with weight loss, but no hemoptysis. Fourteen days before admission she "caught cold." Ten days before admission she had a chill and developed a fever and cough, with brownish sputum. She received sulfapyridine before coming to the hospital, to no avail.

On admission the patient was extremely ill, the temperature was 102°F, the pulse 120, and the respirations 30. There was consolidation of the entire right lung. A diagnosis of tuberculosis and pneumonia was made. Treatment was started with sulfathiazole. A culture of the sputum revealed Type 25 pneumococcus, and a 24-hour

concentrate was negative for tubercle bacilli. The white cell count was 26,100, with 79 per cent polymorphonuclear leukocytes and 18 per cent lymphocytes. X-ray examination revealed consolidation of the entire right lung.

Despite treatment during the next 18 days, the patient ran a continual fever that spiked between 99 and 102°F. She then became suddenly worse, developed signs of meningitis and was found to have a Type 25 pneumococcemia and pneumococcal meningitis. She died 2 days later.

Post-mortem examination showed in addition to purulent meningitis a chronic cavernous tuberculosis in the right upper lobe and unresolved pneumococcal pneumonia in the right lower lobe.

Comment In this case also, although both conditions occurred in an active phase, no evidence of activation or increase in the tuberculosis was demonstrated.

CASE 4 (No 122759) The patient, a 58-year-old man, was well and working until 6 days before admission, when he had a severe chill followed by fever. He soon developed a cough productive of blood-streaked sputum, severe pain in the right upper chest, aggravated by deep inspiration and coughing, and shortness of breath. He had been in good health until the onset of the present illness. There were no prior symptoms referable to the respiratory tract.

Examination on admission showed the patient to be acutely ill. The temperature was 102°F, the pulse 128 and the respirations 68. There was consolidation of the right upper and middle lobes and infiltration in the left upper lobe, and auricular fibrillation. Cultures of the sputum and blood disclosed Type 1 pneumococcus in each. The white-cell count was 33,800, with 88 per cent polymorphonuclear leukocytes. An electrocardiogram confirmed the auricular fibrillation.

The patient was treated with digitalis and sulfadiazine and placed in an oxygen tent. The temperature dropped to normal within 2 days, and remained normal for 3 days, when it began to show a daily afternoon rise. Seven days after admission, the patient was much improved and required no supplementary oxygen, but the consolidation remained over the right upper lobe and anorexia, weakness and productive cough continued. On the 14th day, an electrocardiogram revealed that the auricular fibrillation had given way to a normal rhythm. A chest film showed dense infiltration of both upper lobes, with cavities in both. Three sputum specimens were negative for tubercle bacilli, but a fourth, taken 3 weeks after admission, was positive. The patient was then treated for active tuberculosis. Approximately 1 year after admission and after a left 7-rib thoracoplasty, he was discharged to a sanatorium for continued convalescence.

Comment This case is one in which tuberculosis must have been present and active although the patient was asymptomatic. A definite lobar consolidation with bacteremia occurred in the area of tuberculous infection. Because the patient was symptomless before the pneumonia and had symptoms following it, there was probably definite increase in the tuberculous, but because the exact status of the tuberculous infection prior to the pneumonia is not known, the case is included in the category of probable reactivation.

CASE 5 (No 103042) The patient, a 31-year-old Negress, had been well until 2 weeks prior to admission, when she developed a cough with expectoration, fever and malaise, all of which grew worse until admission. She was subject to "colds," during which she often expectorated blood.

On admission the patient was extremely ill. The temperature was 103°F, the pulse 135, and the respirations 35. There was moderate dyspnea and signs of consolidation of the entire left lung. Sputum and blood cultures both disclosed Type 16 pneumococcus. The white-cell count was 24,600, with 80 per cent polymorphonuclear leukocytes.

Treatment was supportive and consisted of massive doses of Type 16 antiserum. Daily blood cultures remained positive for Type 16 pneumococcus for the next 5 days. The temperature fluctuated between 99 and 103°F for 6 days, when the patient began to run a low-grade fever ranging between normal and 101°F. Because of persistent chest signs, an x-ray film was taken 3 weeks after admission, this revealed soft mottling throughout

if lengthening muscle acquires the tendency to recoil into spasm. During the day, with the patient in the erect or sitting posture, the calf muscles maintain a considerable degree of tone and are in a state of partial contraction against varying degrees of pull. In the recumbent position, however, relaxation and lengthening occur. In muscle already abnormally stimulated by impulses radiating from an irritated segment of the spinal cord lengthening of the muscle constitutes a trigger mechanism sufficient to throw it into spasm. This, Gootnick points out, is nothing more than an exaggeration of the stretch reflex, which is used every time an ankle jerk is elicited by tapping the Achilles tendon. Many patients volunteer the information that they can bring on an attack by extending their legs.

In 1937, Kennedy and Wolf² described the use of quinine for muscle spasm in myotonia. In 1940, Harvey³ pointed out that quinine increases the refractory period of muscle fibers and by reducing the irritability at the myoneural junction decreases the number of stimuli that can reach the muscle fibers. The precise nature of the action of this drug and its relation to acetylcholine and choline esterase remain to be determined. The therapeutic value of quinine in myotonia congenita prompted Moss and Herrmann⁴ to use it for the abolishment of night cramps. Later, Gootnick used it in his series of cases. These are the only reported cases to be found in which this drug was used in the treatment of night cramps. Prior to its employment, calcium salts were generally given. It is difficult to conceive why deficiency of calcium should give localized cramps as seen in this condition. In 2 cases of the present series blood-calcium and blood-phosphorus determinations were within normal limits.

Because of the rarity of this condition in young men, it was decided to investigate these 23 cases to determine the age incidence and compare it with that of previously reported cases, to ascertain pathologic changes existing in this group, and to learn the effect of quinine sulfate as a therapeutic agent.

The average age of these patients was twenty-four years. Moss and Herrmann reported 15 cases of night cramps seen in the Vascular Clinic of the Cincinnati General Hospital. No age tabulation was given, but in 4 cases the ages were fifty-seven, sixty-seven, sixty-nine and sixty-nine. In Gootnick's series the great majority of patients were in the fifth, sixth or seventh decade, and the youngest patient was thirty-eight years old. So far as can be determined these are the only reported series, although isolated cases have been commented on in the literature from time to time.

The installation at which this study was done was utilized for the basic training of troops and for the training of aviation mechanics. Their curriculum included considerable marching and drill, physical training and long hours of standing while at school. No Negro soldiers were included in this series.

There were 2 cases of old, deep, venous thrombosis, 1 of old fracture of the right femur with anterior bowing, 12 of static foot deformity and 8 cases in which no disease could be found. In none of the cases was there any evidence of arterial disease. It was also interesting that many of the patients with static foot deformity presented no symptoms directly referable to it. Table 1 summarizes the duration of symptoms, their location, the incidence of occurrence, the existing pathologic changes and the response to quinine sulfate.

Two patients (Cases 19 and 20) were hospitalized for study. The former had had pneumonia three and a half years prior to admission, complicated by deep thrombophlebitis of the left leg, requiring bed rest for a number of months before resuming activity. Within a few weeks he began to develop typical night cramps in the muscles of the left calf, occurring practically every night. When he rested a good deal he had no cramps. At the time of his induction some eighteen months previously, he had noted the appearance of dilated veins on the lower abdomen and left upper thigh. Since that time the veins in the left leg and upper abdomen had become larger and the cramps occurred three to four times a night. Examination showed dilated upper thigh and lower abdominal veins, but no edema of the extremities. The patient was placed at complete bed rest, and after three days noted complete disappearance of his cramps. Bed rest was continued for three more days, without recurrence. He was then allowed up, and the cramps recurred within forty-eight hours. Quinine sulfate given in an increasing daily dosage of 0.20, 0.32 and 0.50 gm. relieved but did not abolish them.

In Case 20, the patient had had pain in both legs and calf muscles for three years, it developed after extensive standing. Thirteen months before admission he began to have severe night cramps in both calf muscles. Examination revealed a contraction of the hamstring and gastrocnemius muscles and second-degree pes planus. The patient had used orthopedic appliances for his feet, without relief.

He was placed at complete bed rest, with disappearance of the night cramps on the third day and without recurrence during the next three days of rest. On being allowed up he had a recurrence on the second day. Quinine sulfate in doses up to 0.50 gm. at night partially relieved but did not abolish the cramps.

The purpose of placing these patients at complete bed rest was to remove the sources of irritation, which brought relief. This tends to support Gootnick's contention that an irritative source is the primary factor in production of the reflex phenomenon resulting in tetanic contraction of the calf muscles.

In this series we first prescribed 0.20 gm. of quinine sulfate, but later this dose was increased to 0.32 gm., since the larger dose was found to be more

An x-ray film taken on the 20th day showed marked clearing of the consolidation in the right upper lobe and complete clearing in the middle lobe. A repeat film on the 35th day disclosed further clearing in the right upper lobe, so that there remained only a mild hazy infiltration at the right apex, which still had the appearance of a resolving pneumonia. The patient refused to stay in the hospital, and the final outcome of this lesion was never learned.

Comment In this case lobar pneumonia occurred in a lobe that probably contained healed tuberculous lesions. The acute inflammatory process set free some of these organisms from time to time, and they were found in the sputum. For this reason, and because residual shadows persisted for more than 3 weeks, this case is classified as one of doubtful reactivation. It is possible that the healing of the pneumonic process was impaired because the reparative powers of the lung had previously been damaged by the healed tuberculous process.

CASE 10 (No. 130549) The patient, a 32-year-old man, was well until 2 weeks before admission, when he developed a "cold" with a nonproductive cough. One week before admission he experienced chills and fever and pain of a pleuritic type in the right lower anterior chest. A few days prior to entry, the cough became productive of nonbloody sputum. There was no personal or family history of tuberculosis.

On examination the temperature was 104°F, the pulse 108, and the respirations 30. Infiltration was discovered in both upper lobes. The white-cell count was 19,700 with 80 per cent polymorphonuclear leukocytes. Culture of the sputum disclosed pneumococci in abundance, and

a smear for tubercle bacilli as well as a blood culture was negative.

The patient was treated with full doses of sulfamerazine. Although the temperature fell to 99°F within 2 days, it began to spike to 101°F daily for the next 6 days, it then returned to normal. Because of this atypical response of the temperature and because signs persisted in the left upper lobe, an x-ray film was taken 1 week after admission. It showed consolidation in the right upper lobe, and pleural thickening and fibrosis with a cavity beneath the clavicle in the left upper lobe. Soon afterward the sputum was found to be positive for acid-fast organisms. A repeat film taken 1 month later revealed complete resolution of the process in the right upper lobe but no change in the tuberculosis of the left upper lobe. At this point the patient left the hospital against advice, and contact with him was lost.

Comment This case most nearly approaches the type of case sought for — active tuberculosis with superimposed pneumococcal pneumonia, with resolution of the latter and continuation of the active process of tuberculosis. Such cases are the best ones for the study of the two diseases, since they show simultaneous occurrence in the same patient. They clearly demonstrate the occurrence of pneumonia with tuberculosis, but the difficulty in finding such cases just as clearly demonstrates the rarity of the situation.

* * *

In all the above case reports, the sputum studies for tubercle bacilli were made by study of the stained smear of the concentrate of a twenty-four-hour specimen.

NIGHT CRAMPS IN YOUNG MEN

CAPTAIN JOSEPH H. NICHOLSON, M.C., A.U.S., AND CAPTAIN ABRAHAM FALK, M.C., A.U.S.

IT WAS with considerable surprise that we found many young men at an Army Air Force installation who were reporting to the dispensary because of distressing night cramps, since this condition is one usually seen in middle-aged and old people. In the course of nine months, 35 men presented themselves for treatment, in 23 of these cases we are reporting our findings. The remaining 12 patients could not be followed or did not return for a checkup.

Night cramps present a fairly typical clinical picture. It is usually that of a person free of symptoms during the day, whether resting or walking. He retires without symptoms but is awakened by a cramping pain in one or both legs. The calf muscles are hard and tender. These muscles are the ones usually affected, but any muscle group in the lower extremity may be involved. Very rarely muscle groups in other parts of the body are affected. Vigorous rubbing of the leg or hopping about gradually relaxes the muscles, but there is often a residual soreness lasting for hours. Attacks may occur once during the same night or frequently.

The patients are often seen in the Vascular Clinic because they are erroneously considered to be suffering from intermittent claudication, but the differentiation is simple, and they almost invariably have

no peripheral arterial disease. In this series there were 2 patients with pathologic changes in the veins that appeared to be responsible for the attacks of cramps.

Comparatively little investigation of this subject has been done. Gootnick,¹ having studied 30 cases of night cramps in veterans of World War I, has offered an explanation of the causative factors. It is his belief that night cramps are caused by a tetanic contraction of a muscle group due to reflex bombardment of the myoneural junction by a stream of impulses from some neighboring source of irritation. This source may be arthritis of the hip or knee, weak feet or intrinsic inflammatory changes in the nerves or muscles of the extremities. Gootnick thinks that this reaction represents a variety of segmental visceromotor reflex, similar to that seen in visceral inflammation in the abdomen with resulting abdominal rigidity. In night cramps the irritative focus in the spinal cord is not produced by visceral disease but by the changes in the skeletal structure of the same segmental distribution as the muscles affected.

Gootnick also presents an explanation for the occurrence of cramps at night, based on the physiologic fact that the tension of muscle fibers increases as the muscle lengthens and that beyond a certain degree

Despite increased dosage those in Group 3 obtained no relief, although medication was continued for a number of weeks. We believed that increasing the dosage of quinine above 0.32 gm. or continuation of the medication for longer than ten days was not indicated if relief was not obtained in that time.

No definite correlation could be found between the underlying pathologic changes and the response to medication. In Group 1 there were 7 patients in whom no pathologic changes could be found, whereas there was only 1 such patient in Group 2, and none in Group 3. In general one might expect a better therapeutic response in these subjects

DISCUSSION

In contrast to the results obtained by Gootnick, 26 per cent of these patients failed to obtain complete relief from night cramps by the use of quinine sulfate, and the majority of those who obtained relief required a number of doses. The effect of this drug is short-lived and not cumulative, and we are unable to explain why patients should have relief for many days, and not infrequently for weeks, after medication had ceased.

In slightly more than a third of the cases no underlying changes could be found, which raises a question concerning the occurrence of night cramps in apparently normal persons. It may be that these men had lowered muscular strength and general muscular weakness not obvious on routine physical examination or a lower threshold of irritability induced by fatigue from the training program. They were able, however, to keep up with the rest of the troops and to carry on the usual daily routine. No difference could be seen between their general physi-

cal makeup and that of the average healthy soldier. No attempt was made to judge physical endurance or muscular capacity by means of physical-training gradients.

The most frequent disorder predisposing to night cramps was static foot deformity, which occurred in 12 cases. Five of these patients also had symptoms directly referable to the feet. In all these cases orthopedic appliances had been used, with partial relief of foot symptoms but with no change in the occurrence of the night cramps. In none of the patients was there found any peripheral arterial disease, although in 2 cases there was old deep thrombophlebitis of the lower extremities.

SUMMARY AND CONCLUSIONS

Night cramps occur in young men as well as in older people.

Static foot deformity appeared to be the most frequent single predisposing factor in the occurrence of night cramps in this series.

Apparently healthy persons may have night cramps, and yet physical examination may fail to show any defects.

Quinine sulfate offers rapid and frequently complete relief, for varying periods, in a majority of cases.

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practical. In this way it was possible to treat from the start those who required more than the 0.20-gm dosage, and since men on this post were constantly being moved, it afforded a somewhat longer period to observe the effect of adequate dosage. The medication was taken at night, before retiring. No other medications were used.

No attempt was made to correct static foot deformities, and the patients who used orthopedic

The patients were classified in three groups, depending on the response to quinine sulfate.

Group 1 (17 cases) included those who obtained complete relief, Group 2 (3 cases) included those who obtained partial relief, and Group 3 (3 cases) included those who obtained no relief.

All those who responded well to quinine did so within a period of seven days of medication. Four patients in Group 1 had a recurrence of symptoms

TABLE 1 Summary of Data

CASE No.	AGE yr	PATHOLOGIC CHANGE	INVOLVEMENT*	DURATION	FREQUENCY	INITIAL DOSAGE OF QUININE gr	RESULTS
GROUP 1							
1	57	Old left thrombophlebitis	Left	16 yr	Nightly	0.32	Relief after 5th dose; no recurrence in 1 month.
2	24	First-degree pes planus	Bilateral	2 mo	Nightly	0.32	Relief after 2nd dose; no recurrence in 1 month.
3	18	First-degree pes planus	Bilateral	2 yr	Nightly	0.20	Relief after 1st dose; no recurrence in 2 months.
4	27	Old fracture of right femur with anterior bowing	Right	4 mo	Nightly	0.20	No relief in 1 week; dosage increased to 0.32 gm., with relief after 3rd dose; no recurrence in 2 weeks.
5	52	Third-degree pes planus	Bilateral	1 yr	Nightly	0.20	Relief after 7th dose; one slight attack in next 3 weeks.
6	24	First-degree pes planus	Bilateral	3 mo	Nightly	0.32	Relief after 3rd dose; no recurrence in 2 weeks.
7	28	None	Bilateral	5 yr	Nightly	0.32	Relief after 5th dose; no further check.
8	19	None	Bilateral	2 yr	Nightly	0.20	Relief after 3rd dose; no recurrence in 1 month.
9	19	None	Bilateral	2 yr	Nightly	0.32	Relief after 6th dose; no recurrence in 3 weeks.
10	22	None	Bilateral	5 mo.	Nightly	0.20	Relief after 4th dose; no recurrence in 1 week.
11	25	None	Bilateral	3 mo.	Nightly	0.20	Relief after 5th dose; no recurrence in 1 month.
12	19	None	Bilateral	3 mo	Nightly	0.32	Relief after 2nd dose; no further check.
13	25	None	Bilateral	3 yr	Nightly	0.32	Relief after 4th dose; no further check.
14	19	Third-degree pes planus	Bilateral	3 yr	Nightly	0.20	Relief after 4th dose; recurrence in 2 weeks; resumption of dosage brought relief after 5th dose; no recurrence in 2 weeks.
15	16	Second-degree pes planus	Bilateral	10 mo	Nightly	0.20	Partial relief after 1 week; dosage increased to 0.32 gm., with complete relief after 5th dose; no recurrence in 2 weeks.
16	27	Second-degree pes planus	Bilateral	5 yr	Nightly	0.20	Partial relief after 1 week; dosage increased to 0.32 gm., with complete relief after 4th dose; no recurrence in 2 weeks.
17	55	Metatarsalgia	Bilateral	3 wk.	Nightly	0.32	Relief after 5th dose; recurrence 7 days later; dosage decreased to 0.20 gm., with relief after 5th dose; no recurrence in 2 weeks.
GROUP 2							
18	24	None	Bilateral	5 mo	Nightly	0.20	Partial relief; dosage increased to 0.32 gm., then to 0.49 gm., without further effect.
19	25	Old left thrombophlebitis	Left	3 yr	Nightly	0.20	Partial relief; dosage increased to 0.65 gm., without further effect.
20	55	Second-degree pes planus right hamstring and calf muscles bilaterally	Bilateral (calf and thigh)	13 mo	Nightly	0.20	Partial relief; dosage increased to 0.65 gm., without further effect.
GROUP 3							
21	18	Second-degree pes planus	Bilateral	5 mo	Nightly	0.20	No relief after 7th dose; dosage increased to 0.49 gm., without relief after 3 weeks of medication.
22	21	First-degree pes planus	Bilateral	1 yr	Nightly	0.32	No relief; dosage increased to 0.65 gm., without relief after 2 weeks of medication.
23	25	Second-degree pes planus	Bilateral	3 mo	Nightly	0.32	No relief; dosage increased to 0.49 gm., without relief after 3 weeks of medication.

*Unless otherwise indicated refers to calf muscles.

appliances were allowed to continue them. Those who had varicosities were given no surgical or other treatment for relief. All the men were informed that they were to keep up their normal activities. The 2 hospitalized cases were followed prior to admission, and the results listed are those secured prior to hospitalization. All the patients were told to report in one week and were instructed to discontinue medication on relief of the cramps and to report the number of days of medication required for this result.

within two weeks after stopping the medication. In those who could not be followed for longer periods it was not possible to determine the incidence of recurrences. Five patients followed for one month and 1 followed for two months remained asymptomatic. In the cases in which there was a recurrence, relief was obtained in each case when quinine sulfate was again given.

Three patients in Group 2 obtained only partial relief, but the night cramps became less intense and less frequent. Increasing the dosage had no added effect.

Despite increased dosage those in Group 3 obtained no relief, although medication was continued for a number of weeks. We believed that increasing the dosage of quinine above 0.32 gm. or continuation of the medication for longer than ten days was not indicated if relief was not obtained in that time.

No definite correlation could be found between the underlying pathologic changes and the response to medication. In Group 1 there were 7 patients in whom no pathologic changes could be found, whereas there was only 1 such patient in Group 2, and none in Group 3. In general one might expect a better therapeutic response in these subjects.

DISCUSSION

In contrast to the results obtained by Gootnick, 26 per cent of these patients failed to obtain complete relief from night cramps by the use of quinine sulfate, and the majority of those who obtained relief required a number of doses. The effect of this drug is short-lived and not cumulative, and we are unable to explain why patients should have relief for many days, and not infrequently for weeks, after medication had ceased.

In slightly more than a third of the cases no underlying changes could be found, which raises a question concerning the occurrence of night cramps in apparently normal persons. It may be that these men had lowered muscular strength and general muscular weakness not obvious on routine physical examination or a lower threshold of irritability induced by fatigue from the training program. They were able, however, to keep up with the rest of the troops and to carry on the usual daily routine. No difference could be seen between their general physi-

cal makeup and that of the average healthy soldier. No attempt was made to judge physical endurance or muscular capacity by means of physical-training gradients.

The most frequent disorder predisposing to night cramps was static foot deformity, which occurred in 12 cases. Five of these patients also had symptoms directly referable to the feet. In all these cases orthopedic appliances had been used, with partial relief of foot symptoms but with no change in the occurrence of the night cramps. In none of the patients was there found any peripheral arterial disease, although in 2 cases there was old deep thrombophlebitis of the lower extremities.

SUMMARY AND CONCLUSIONS

Night cramps occur in young men as well as in older people.

Static foot deformity appeared to be the most frequent single predisposing factor in the occurrence of night cramps in this series.

Apparently healthy persons may have night cramps, and yet physical examination may fail to show any defects.

Quinine sulfate offers rapid and frequently complete relief, for varying periods, in a majority of cases.

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MEDICAL PROGRESS

THE EFFECTS OF INFECTION ON THE CIRCULATION*

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THERE are many ways in which infection may give rise to circulatory disturbances, and it is the purpose of the present report to discuss the pathologic physiology of these disorders.

A large number of infectious diseases, some still of doubtful etiology, give rise to vascular lesions. Included in this group are rheumatic fever, syphilis, Fiedler's myocarditis, acute disseminated lupus erythematosus, periarteritis nodosa, mycotic aneurysms, acute and subacute bacterial endocarditis, typhus fever and meningococcemia. Similarly, the various urticarias, purpuras and macular or papular rashes also represent the effects of vascular lesions. It is not our purpose to describe the pathologic anatomy of any of these, it is sufficient merely to call attention to the fact that some infections give rise to anatomic changes involving the cardiovascular system. A functional disorder of the cardiovascular system that may occur in association with infectious processes is arrhythmia of the heart. The heart block of diphtheria, the prolonged PR interval of rheumatic fever and other infections and the transitory auricular fibrillation associated with pneumonia in the aged are too well known to require emphasis in the present work.

Fever

Another way by which cardiovascular physiology may be influenced during the course of infectious processes is through the occurrence of fever. Although the importance of fever as a symptom of infectious disease has been known since the time of Hippocrates, appreciation of the physiologic mechanisms that result in the circulatory and respiratory manifestations of fever is not widespread among clinicians. Studies of fever consequent on the intravenous injection of killed typhoid bacilli or live malarial parasites^{1, 2} make it clear that the febrile reaction consists in phases that are fairly sharply defined and that follow in regular sequence. The clinical appearance of the patient is distinctive, and the various cardiorespiratory functions that have been measured likewise show different changes in each phase. The phases have been termed "prodrome," "chill," "flush" and "defervescence."

The prodrome begins soon after the endovenous injection of the typhoid vaccine, lasts thirty to ninety minutes and is characterized by lassitude, headache, generalized aches and pains, and malaise. Measurements of cardiac output, venous pressure, circulation time, pulse rate, blood pressure, vital capacity, respiratory rate, oxygen consumption, respiratory minute volume, respiratory quotient, arterial and venous oxygen and carbon dioxide content, arterial pH and blood volume show no significant changes from control values, electrocardiographic tracings reveal no deviation from the normal. Direct observation of the cutaneous capillaries in the fingernail bed shows no changes in caliber or flow.

The mechanisms responsible for the prodromal period and the symptoms observed are not understood. Although it is assumed that antigen-antibody reactions are probably taking place, no clear evidence exists for their presence. In this connection it should be mentioned that many observers have induced fever in animals and in human subjects with purified proteins or polysaccharides obtained from bacteria or exudates.³⁻⁷ In all these instances a prodromal period is present.

The chill phase begins suddenly. The patient becomes pale and cyanotic, and goose flesh may be observed. The skin is, however, dry except that a few beads of perspiration become visible on the forehead or upper lip. The superficial veins become visibly narrow, and withdrawal of blood from them may be difficult. Obvious hyperventilation occurs. Nausea is a complaint in almost all patients, and some vomit. Excretion of urine is minimal or absent during this phase. The rectal temperature rises rapidly but the skin remains cool. The patients complain of feeling cold and many shiver, in some cases severe shaking chills occur. The latter can be precipitated in the chill phase by exposing the patient to a blast of cool air or by placing a small piece of ice in his hand. Conversely external heat and blankets minimize the shivering of the chill. The dynamic changes occurring during the chill phase last from one to two hours. The capillaries of the nailfold rapidly disappear, and the few that remain visible are markedly narrowed and contain blood that moves slowly. The columns of blood within the capillaries appear segmented. The systolic and diastolic levels of arterial blood pressure tend to rise in the early part of the chill phase, but in some cases, a marked fall in blood pressure

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cur, a point that will be discussed further below. The antecubital venous pressure measured directly, usually shows no striking change, but a fall in venous pressure occurs in some cases. The arteriovenous oxygen difference increases during the chill phase, with a marked fall in venous blood oxygen content. Changes in cardiac output are variable in the chill phase, the cardiac output often falls, whereas in the remainder of the cases the increases in cardiac output are smaller than what would be expected from the observed changes in oxygen consumption. Slowing of the arm-to-tongue circulation time occurs in almost all patients during the chill phase, the degree of slowing varying with the severity of the chill reaction. The pulse rate rises approximately ten beats per minute for each degree rise in rectal temperature.⁸⁻¹⁰ When rigors or muscle tensing is absent, the oxygen consumption varies roughly with the rectal temperature, increasing approximately 7 per cent for each degree of fever.¹¹⁻¹³ The respiratory minute volume rises during the chill phase, the increase exceeding that of oxygen consumption. The increase in respiratory rate, greater than that of the minute-volume respiration, results in a decrease in tidal air. The alveolar-air carbon dioxide content and the arterial carbon dioxide level fall during the chill phase, and the arterial blood pH rises slightly. The respiratory quotient is increased.^{1, 12} In severe chill reactions, an increase in residual air may be observed, indicating some degree of pulmonary congestion. A fall in reserve and complementary air and in vital capacity is seen in such cases. Changes in the oxygen saturation of the arterial blood, however, are small. The blood volume is unchanged.^{1, 14} Aside from the observed increase in pulse rate, the electrocardiograms showed flattening of the T waves late in the chill phase.

It is apparent from these observations and from others in the literature that the chill phase is associated with the onset of marked generalized vasoconstriction, which is visible in the skin and nailfold capillaries and is also probably present in the kidneys and brain. In 1883 Mendelson¹⁵ demonstrated during fever in dogs a progressive shrinkage in the size of the kidneys, which he attributed to arterial constriction, and Fremont-Smith et al.¹⁶ showed that the chill phase induced by typhoid vaccine, malaria and rat-bite fever was associated with a cessation of urine formation. Recently, Smith et al.¹⁷ showed that the chill phase of typhoid vaccine fever is accompanied by a 25 per cent reduction in renal blood flow. It is of interest that the previous administration of pyramidon abolished the febrile reaction but did not prevent the renal vasomotor changes. The studies of Himwich et al.¹⁸ showing an increased arteriovenous oxygen difference in cerebral blood, suggest that the brain participates in the circulatory stagnation of the chill phase. Since the circulating blood volume shows no change, it is apparent that there must be

areas in the body that are not the seat of generalized vasoconstriction and may be the site of vasodilatation. The increase in the residual air volume and in the ratio of the residual air to the total pulmonary capacity in the chill phase suggests that some degree of pulmonary congestion may occur. It is of some interest in this respect that Sprunt and Camaher¹⁹ have shown the occurrence of edema and congestion of the lung of rabbits and men following the injection of staphylococcal and other toxins. That the observed vasoconstriction is nervous in origin is apparent from the studies of Johnson, Osborne and Scupham²⁰ and Perera,²¹ who observed no vasoconstriction in a denervated limb. In 1927, von Euler²² described a substance in the blood of patients with fever that had vasoconstrictor effects and also gave colorimetric reactions suggesting that it was adrenalin. It should be stressed that the observed changes in skin circulation in the chill phase are the same as those that occur with externally applied cold, thus, the cutaneous vasoconstriction of exposure to cold is associated with narrowed veins, a decreased rate of circulation, a decreased oxygen content and a fall in skin temperature, which, when it reaches a sufficiently low level,²³ results in shivering or muscle tenseness. Furthermore, with the increased heat production and the inability to lose heat through the skin, the internal body temperature rises. The severer the chill, the greater the rise in body temperature. Once the circulating blood within the skin and brain rises to a certain level, relaxation of local vasoconstriction and central stimulation of vasodilator fibers occur, which ushers in the flush phase.

The observed decreases in cardiac output are probably not related to a direct depression of cardiac function, since bradycardia does not occur, and since the tachycardia of fever ordinarily does not reach levels, that is, 180 per minute or above,²⁴ that might give rise to a lowering of cardiac output by markedly shortening diastole. Furthermore, measurements of the venous pressure never show an increase. Thus the changes observed in cardiac output during the chill phase are a resultant of the tendency to rise with the increasing oxygen consumption and the tendency to fall with the impairment of venous return that is probably present. The changes in circulation time are probably related to cutaneous vasoconstriction, since Stead and Kunkel²⁵ have shown that simple cooling of the skin may comparably slow the arm-to-tongue circulation time.

The mechanisms responsible for the excessive hyperventilation of the chill phase are as follows: limitation of heat dispersal due to cutaneous vasoconstriction, increased temperature within the brain, which is known to give rise to hyperventilation,²⁶⁻²⁸ the latter being a mechanism for heat dispersal, anoxia, which occurs when the cardiac output falls and pulmonary congestion, which

may activate reflexes within the lungs, thus producing excessive hyperventilation. The observed hyperventilation is responsible in part for the rise in the respiratory quotient, although the probability exists that an increase in carbohydrate utilization with increased fever may be a factor. The alkalosis that results from the observed hyperventilation may be responsible for the occurrence of convulsions in children, the fact that the alkalosis is not marked is probably due to the observed elevation of fixed acids, namely, lactate and pyruvate, within the blood.²⁹

The flush phase of the febrile reaction is characterized by the rapid development of a generalized flush and a drenching sweat. The patient suddenly complains of feeling warm, and the skin is hot, the superficial veins become markedly dilated. A pounding headache occurs, and complete relief of nausea and vomiting is noted. The onset of the flush phase is usually associated with a diuresis. This phase lasts for approximately one hour and then passes into the phase of defervescence, the abnormal findings in the flush phase gradually regressing over a period of several hours.

The physiologic changes in the flush phase are manifold. There is a rapid appearance of large numbers of widely open capillaries in the fingernail beds, containing blood moving rapidly. All visible vessels, including arterioles and venules, appear to pulsate. The arterial blood pressure, both systolic and diastolic, shows a fall, but the venous pressure remains unchanged or rises a little. The circulation time is uniformly decreased, and the cardiac output increases markedly and in excess of what would be accounted for by the observed increase in oxygen consumption. As a consequence, the arteriovenous oxygen difference falls, and the venous oxygen content rises almost to the arterial level. The respiratory minute volume increases, but the respiratory volume relative to oxygen consumption per minute falls to or toward normal. The rate of respiration decreases somewhat, as compared to the respiratory minute volume, and the tidal-air volume usually increases. The alveolar-air carbon dioxide content remains low, and the arterial pH remains elevated, both return toward control levels during defervescence. The blood volume is unchanged. Electrocardiograms taken during the flush phase usually show inversion of T waves, unassociated with changes in the ST segment.

The marked generalized vasodilatation initiated in the flush phase probably involves not only the capillaries but also the arterioles and arteriovenous shunts. The latter is likely, since venous blood becomes arterialized and slight rises in venous pressure are observed. The excessive increases in cardiac output are probably related also to opening of arteriovenous shunts, with an increased venous return, and perhaps also to elevated cerebral temperatures.²⁷ Nevertheless, there must be areas of

compensatory vasoconstriction, since the blood volume is not changed.

The sudden vasodilatation observed in the flush phase probably involves a neurogenic mechanism¹ activated by increased warmth of the blood within the brain, with resultant stimulation of vasodilatation centers. Gibbon and Landis³⁰ have shown that increased temperature of the blood within the brain produces a generalized vasodilatation, furthermore, a sympathectomized extremity does not exhibit vasodilatation when the body is heated. It is of interest that Hewlett³¹ has shown that a previously chilled extremity, when warmed, does not show an increased flow until the external temperature has been considerably elevated. It is thus possible that the local circulation of sufficiently warm blood may relax vasoconstriction. The elevation of pulse rate is probably due to increased warmth of the blood supplying the sinoauricular node,^{32, 33} although the possibility exists that central stimulation is a factor.²⁶

The duration and severity of the four phases of a febrile reaction may vary greatly in various infectious diseases. Thus, in a patient with untreated pneumococcal pneumonia, the moderately severe chill phase of a few hours may be followed by a flush lasting more than a week, this being in turn followed by defervescence over a period of a few hours or a few days. In typhoid fever, on the other hand, a prodromal period of one to two weeks may occur, followed by a week of successive elevation and partial lowering of temperature, which may be compatible with many chill and flush phases followed by a long flush period of several weeks. In a patient with a septic process or malaria, severe chill and flush phases of approximately equal duration may occur daily. It is apparent that, under these circumstances, many factors as yet not understood unquestionably modify the above described manifestations of the febrile reaction.

Thiamine Deficiency

The development of thiamine deficiency in patient with infectious diseases of long duration is well known. Accordingly, the circulatory manifestation of fever may be modified by the changes in cardiovascular dynamics consequent to vitamin B₁ deficiency. The available data,³⁴ although scanty suggest that thiamine deficiency in man is associated with a relative increase in cardiac output as compared to the oxygen consumed, a decrease in the circulation time, an increase in the oxygen consumption, an increase in the circulating blood volume and an elevated venous pressure. There is a decreased arteriovenous oxygen difference, and with the decreased circulation time, there is thus suggested the presence of an abnormally dilated peripheral vascular bed. The cardiovascular change of the chill phase of fever might be somewhat diminished, whereas the phenomena of the flush phase

might tend to be accentuated in the presence of thiamine deficiency. In addition, a deficiency of this vitamin resulting from a protracted infection might give rise to congestive heart failure.

Anemia

Severe anemias not infrequently develop during the course of infectious disease. Anemias increase the cardiac output, lower the arteriovenous oxygen difference and accelerate the circulation time. Anemia therefore superimposes an additional strain on the heart beyond that caused by fever. It should be noted in addition that anemic patients show cutaneous vasoconstriction, probably of sympathetic origin, and that patients with pernicious anemia or indeed any severe anemia frequently present elevations of body temperature.

Congestive Heart Failure

The burden placed on the heart by fever may, after a time, cause a previously damaged heart to fail. The contributing roles of anemia and thiamine deficiency have already been noted. The development of signs of myocardial insufficiency during infections in elderly or cardiac patients is well known. All patients in uncomplicated congestive failure exhibit peripheral vasoconstriction, with consequent impairment of heat dispersal, and indeed some such patients exhibit slight elevations of body temperature. This impairment of heat dispersal through the skin may give rise to severe dyspnea in the presence of fever. It is of interest that Buchbinder and Saphir³⁵ observed the pathologic changes of congestive heart failure in approximately half of a large series of patients with subacute bacterial endocarditis.

Rashes

The vasomotor manifestations of fever are of interest in relation to the occurrence of disappearance of erythematous rashes. Thus the cutaneous vasoconstriction of a severe chill may cause a rash to disappear or become darker in hue. On the other hand, an extremely severe flush may mask a macular erythema to some extent.

Postinfectious Asthenia

It is a striking clinical observation that patients who have recovered from short febrile illnesses may be excessively weak and tired. They often exhibit profuse and easy sweating and such marked vasomotor instability that postural syncope occurs. These symptoms may last for considerable periods of time and may be far more incapacitating than the illness that they followed. Although the cause of this postinfectious syndrome has not been completely elucidated, certain of the phenomena are explainable. It is known that fever causes certain biochemical changes similar to those of trauma, myocardial infarction and burns, that is, a markedly

negative nitrogen balance and creatinuria³⁶⁻³⁸; these changes may be associated with obvious muscular wasting. It is also apparent from the data cited above that a febrile illness gives rise to a considerable degree of stress on the centers controlling vasomotor, cardiomotor, respiratory and sweating functions, which might result in prolonged instability in the function of these centers.

Infectious Shock

Shock consequent to trauma and hemorrhage has been widely investigated, but few data are available in shock due to infection. The clinical manifestations of shock, whatever the etiology of the latter, are more easily recognized than described. The appearance of the patient in shock associated with an infection is similar to that of the patient in an extremely severe chill phase, one difference between the two is the fact that the rectal temperature rises during the chill phase of fever, whereas it may not rise, and indeed may fall to subnormal levels, in infectious shock. It is of interest that shock in infections occurs early in the course of the disease; for example, patients with meningococcemia may develop peripheral vascular collapse before signs of meningitis have appeared^{39, 40}. Shock may likewise be the presenting symptom in postoperative wound infections,⁴¹ peritonitis,⁴² acute bacillary dysentery,⁴³ scarlet fever,³⁹ and acute pneumococcal pneumonia.³⁹ In addition, the studies of Aub et al.⁴⁴ and of Prinzmetal et al.⁴⁵ suggest that shock due to tourniquets or crush injury in dogs may be largely consequent to infection. A large volume of clinical data based on observation of patients and also on the response to digitalis bodies and to fluids and various sympathomimetic substances has convinced clinicians that infectious shock is not related to cardiac failure but to some disturbance of the peripheral circulatory apparatus.

Measurements of circulation. As mentioned above the clinical picture of shock develops in some patients during the chill phase of the febrile reaction to typhoid vaccine. This is associated with a low cardiac output, an increased arteriovenous oxygen difference, deoxygenation of the venous blood and a low arterial blood pressure. The circulating blood volume is unchanged, however, and oxygen consumption and rectal temperatures do not fall. It is pertinent to point out that the cutaneous manifestations of vasoconstriction — that is, cold, clammy extremities, blanched mucous membranes, cutis marmorata and venous constriction — are present in the chill phase of the febrile reaction as well as in infectious shock. In both instances these phenomena are neurogenic in origin. In patients with infectious shock, ulnar-nerve block with procaine results in increased warmth of the involved fingers.⁴⁶ Many years ago Freedlander and Lenhart⁴⁷ described capillary constriction and slowed flow in the skin of the nailfold of patients in shock consequent to

infection Ebert and Stead⁴⁶ studied 8 cases of circulatory failure in infections, 6 of which were due to pneumococcal pneumonia. In none was the circulating plasma volume significantly altered. The absence of elevation of venous pressure rules out a primary cardiac failure.⁴⁶ Eppinger and Schürmeyer,⁴⁸ on the other hand, noted a decreased circulating blood volume in infectious shock. The observations of Rutstein et al.⁴⁹ on the plasma volume and the so-called "extravascular thiocyanate space" in pneumonia show an increase in these values during the illness, with a decrease below normal immediately following recovery. In fatal cases the values were significantly lower than in the patients who survived. These workers correlated the lowered plasma volume with the clinical occurrence of peripheral circulatory failure. The difference in methods employed is not sufficient to explain these discordant results.

Studies have been made of the cardiovascular dynamics consequent to the intravenous injection of various bacterial toxins in unanesthetized dogs.³ The clinical appearance of these dogs resembled closely the shock state, pallor of the mucous membranes, narrowed veins, hyperventilation, anuria, insensibility to pain and general apathy having been observed. Within fifteen to thirty minutes after the injection of Shiga toxin, a decrease in cardiac minute volume output of 25 to 75 per cent occurred. This change was associated with an increased arteriovenous oxygen difference, marked deoxygenation of the venous blood and a concomitant decrease in the right auricular pressure, the portal venous pressure, however, rose. The latter change was probably due to spasm occurring in the hepatic veins,⁵⁰ with a resultant decrease in venous return from the splanchnic bed, but it is unlikely that this mechanism exists in human beings. The arterial blood pressure was maintained, indicating peripheral vasoconstriction, and evidence of hemoconcentration was absent. During the succeeding hours, despite at times considerable rises in body temperature and severe shivering, the cardiac output persistently decreased and the circulation time became greatly slowed. The portal venous pressure fell to levels considerably below control values. The oxygen consumption increased parallel to the rising body temperature, but both fell when the animal was in deep shock. Decreases in blood volume and increases in viscosity became manifest in two thirds of the dogs late in shock. The late blood-pressure changes were variable. In some animals, the blood pressure rose with the rising body temperature, until the latter reached its peak, when a precipitous fall in blood pressure occurred. It is apparent from the data given above that in these animals vasodilatation associated with the flush phase had set in. In others, a fall in blood pressure to 40 or 50 mm. occurred after one or two hours. This is a counterpart of the fall in blood

pressure observed in the chill phase of some human experiments. It should be noted in this regard that recently Warren et al.³⁹ described 3 cases of infectious shock that illustrate perfectly this type of reaction. Their conclusion that the mechanism of shock is related to a pooling of blood in dilated capillaries, and therefore an uncompensated increase in the size of the vascular bed, with a concomitant reduction in venous return to the heart and in cardiac output, implies that there was a decrease in circulating blood volume. The studies of Ebert and Stead⁴⁶ and our^{1, 2} observations, both in human beings and in animals, do not support this conclusion.

Comparison of circulatory dynamics in infectious shock and in shock due to trauma and hemorrhage. Toxic or infectious shock is similar to experimental traumatic and hemorrhagic shock in the occurrence of a fall in cardiac output and central venous pressure, an increase in the arteriovenous oxygen difference, a marked fall in the venous oxygen content, a slowing of the circulation, a decrease in oxygen consumption, a fall in the arterial blood pressure and an early increase, followed by a late fall, in peripheral resistance. Toxic or infectious shock differs from traumatic or hemorrhagic shock in two respects: the occurrence of fever, with its specific effects on blood pressure, cardiac output and oxygen consumption, and the fact that oligemia is not the initiating mechanism in at least some types of infectious shock. The occurrence of the latter, whether due to dehydration or loss of plasma or blood, is of serious consequence in infectious shock.

Factors influencing occurrence of infectious shock. The occurrence of severe diarrhea in cholera, bacillary dysentery, ulcerative colitis and so forth may induce such dehydration and contraction of the circulating blood volume that they are of considerable significance in the precipitation of shock. Whether the cardiovascular dynamics in such patients differ from those observed in nonoligemic shock is not known.

Andrews and Harkins⁵¹ measured the weight of pneumonic lungs and concluded that sufficient plasma and blood is lost to account for the occurrence of shock on an oligemic basis. As has been pointed out above, measurements of the circulating blood volume in shock and pneumonia have presented conflicting results. Other examples of rapid loss of plasma in infections are offered by phlegmonous areas and pleural empyema. It should be noted that, although the amount of plasma loss alone may not be sufficient to account for the induction of shock, it is certainly a deleterious factor. In 1920 Lautenschläger⁵² analyzed the effects of the intravenous injection of unconcentrated filtrates of cultures of *Clostridium septicum* and concluded that the circulatory collapse so induced was due to a cardiotoxic digitalis-like effect of the toxin. More recent studies by other investigators have

emonstrated a toxic effect on the heart, as well as constriction of the pulmonary and coronary vessels.⁵⁴ Studies on staphylococcal^{54, 55} and streptococcal⁵⁶ toxins likewise show a direct cardiotoxic action. Bernheimer and Cantoni⁵⁸ suggest that the cardiotoxic factor of *Streptococcus pyogenes* is closely related to and perhaps identical with the oxygen-labile hemolysin of the streptococcus. In all the above experiments enormous doses of toxin were used. On the other hand, in dogs in shock after the intravenous injection of Shiga toxin, the administration intravenously of large infusions resulted in a moderate increase in cardiac output and in no abnormal rise in venous pressure³; these findings were taken to indicate that the heart responds normally to increased venous pressure. It should be noted, however, that after such infusions the cardiac output did not rise quite to the control value and soon returned to the preinfusion level. In addition, the absence of any beneficial clinical action of digitalis suggests the absence of a significant cardiac factor in infectious shock. That the heart may be damaged by the presence of shock is well established; Blumgart et al.⁵⁷ found thrombotic occlusion of the coronary arteries in patients who died of shock due to diverse causes.

The Waterhouse-Friderichsen syndrome is described as an infectious disease, occurring mainly in children, that is characterized by a purpuric syndrome involving the skin and adrenal glands and by a severe and almost uniformly fatal shock. In most of the recorded cases, meningococcal bacteremia has been found, although isolated cases of hemolytic streptococcus, staphylococcal and pneumococcal bacteremia have been described. Rich⁵⁸ and others,⁵⁹ however, have described adrenal lesions in infectious shock of diverse origin, and hemorrhages within the cortices of the adrenal gland were found at autopsy in many animals injected with the protein fraction of Shiga bacilli.⁵⁹ It is to be noted that except for the rash, the clinical picture is not at all unlike severe experimental or clinical infectious shock. D'Agati and Marangoni⁶⁰ recently concluded that the difference between meningococcemia complicated by collapse and the Waterhouse-Friderichsen syndrome is the absence in the former of anuria, oliguria and the retention of nitrogenous products. These considerations, however, have no validity, for in every type of peripheral vascular collapse so far studied, and also in the chill phase of fever, renal excretory function practically ceases.

Dale and Evans⁶¹ showed that the activity of the vasomotor center is regulated by the concentration of carbon dioxide in the blood, and it is well known that hyperventilation may cause a transient fall in blood pressure if enough carbon dioxide is blown off. Henderson⁶² believed that hypocarbia is an important factor in the genesis of shock. In our experience, however, the degree of

hypocarbia necessary to cause significant hypotension is so marked as to rule hyperventilation out as the primary cause of the fall in blood pressure seen in infectious shock.³ It may possibly be a contributory factor in some cases.

The studies of Porter⁶⁴⁻⁶⁶ and others^{67, 68} show no impairment of the function of the vasomotor center in infectious shock.

Moon⁶⁹ has described shock as due to widespread capillary dilatation and increased permeability. The evidence that infections cause increased capillary permeability largely consists of Moon's pathological studies showing visceral engorgement in infectious shock. This type of evidence is inconclusive, since visceral engorgement may be an effect of shock rather than a causative factor. Duran-Reynals⁷⁰ reviewed the role of the so-called "spreading factors" in giving rise to local increases in capillary permeability in inflamed areas, and Menkin⁷¹ ascribed these changes to "leukotaxine," a non-protein nitrogenous substance present in exudates. As pointed out above, however, these phenomena are not important in the genesis of infectious shock unless the inflamed area is so extensive that a large loss of plasma from the circulation results. No conclusive evidence exists that a generalized increase in capillary permeability is present in infectious shock.

Therapy of Peripheral Vascular Collapse in Infection

In general, the therapy of infectious shock is most unsatisfactory, and in almost all fatal cases the patients die of or with shock. Atchley,⁷² Eggleston⁷³ and Warfield⁷⁴ have discussed the treatment of this type of shock, and certain general principles should be stressed. The prevention of the development of shock by the early recognition and treatment of disease is of primary importance. If shock is already in evidence when the patient is first seen, the use of adequate amounts of plasma given intravenously is necessary to keep the patient alive long enough for specific serums or antibiotic substances to act, if the latter are not given, plasma infusions have only a temporary beneficial effect. Pressor drugs are ineffective in the presence of infectious shock when given alone,⁷⁵ but when used together with plasma, they regain their effectiveness.

Cardiovascular Complications of Treatment of Infection

Symptoms relating to cardiac and vascular function may be greatly modified in a deleterious manner by treatment. Thus, the purpuras and urticarias of antibiotic or other therapy, the anaphylactic reactions of serum therapy and the pulmonary or peripheral edema following infusions may be more alarming than the infections for which they are employed. These complications may be avoided, or at least minimized by careful treatment. In some cases, induced fever is used to treat low-grade

infection Ebert and Stead⁴⁶ studied 8 cases of circulatory failure in infections, 6 of which were due to pneumococcal pneumonia. In none was the circulating plasma volume significantly altered. The absence of elevation of venous pressure rules out a primary cardiac failure.⁴⁶ Eppinger and Schürmeyer,⁴⁸ on the other hand, noted a decreased circulating blood volume in infectious shock. The observations of Rutstein et al⁴⁹ on the plasma volume and the so-called "extravascular thiocyanate space" in pneumonia show an increase in these values during the illness, with a decrease below normal immediately following recovery. In fatal cases the values were significantly lower than in the patients who survived. These workers correlated the lowered plasma volume with the clinical occurrence of peripheral circulatory failure. The difference in methods employed is not sufficient to explain these discordant results.

Studies have been made of the cardiovascular dynamics consequent to the intravenous injection of various bacterial toxins in unanesthetized dogs.⁵ The clinical appearance of these dogs resembled closely the shock state, pallor of the mucous membranes, narrowed veins, hyperventilation, anuria, insensibility to pain and general apathy having been observed. Within fifteen to thirty minutes after the injection of Shiga toxin, a decrease in cardiac minute volume output of 25 to 75 per cent occurred. This change was associated with an increased arteriovenous oxygen difference, marked deoxygenation of the venous blood and a concomitant decrease in the right auricular pressure, the portal venous pressure, however, rose. The latter change was probably due to spasm occurring in the hepatic veins,⁵⁰ with a resultant decrease in venous return from the splanchnic bed, but it is unlikely that this mechanism exists in human beings. The arterial blood pressure was maintained, indicating peripheral vasoconstriction, and evidence of hemoconcentration was absent. During the succeeding hours, despite at times considerable rises in body temperature and severe shivering, the cardiac output persistently decreased and the circulation time became greatly slowed. The portal venous pressure fell to levels considerably below control values. The oxygen consumption increased parallel to the rising body temperature, but both fell when the animal was in deep shock. Decreases in blood volume and increases in viscosity became manifest in two thirds of the dogs late in shock. The late blood-pressure changes were variable. In some animals, the blood pressure rose with the rising body temperature, until the latter reached its peak, when a precipitous fall in blood pressure occurred. It is apparent from the data given above that in these animals vasodilatation associated with the flush phase had set in. In others, a fall in blood pressure to 40 or 50 mm. occurred after one or two hours. This is a counterpart of the fall in blood

pressure observed in the chill phase of some human experiments. It should be noted in this regard that recently Warren et al³⁹ described 3 cases of infectious shock that illustrate perfectly this type of reaction. Their conclusion that the mechanism of shock is related to a pooling of blood in dilated capillaries, and therefore an uncompensated increase in the size of the vascular bed, with a concomitant reduction in venous return to the heart and in cardiac output, implies that there was a decrease in circulating blood volume. The studies of Ebert and Stead⁴⁶ and our^{1, 2} observations, both in human beings and in animals, do not support this conclusion.

Comparison of circulatory dynamics in infectious shock and in shock due to trauma and hemorrhage. Toxic or infectious shock is similar to experimental traumatic and hemorrhagic shock in the occurrence of a fall in cardiac output and central venous pressure, an increase in the arteriovenous oxygen difference, a marked fall in the venous oxygen content, a slowing of the circulation, a decrease in oxygen consumption, a fall in the arterial blood pressure and an early increase, followed by a late fall, in peripheral resistance. Toxic or infectious shock differs from traumatic or hemorrhagic shock in two respects: the occurrence of fever, with its specific effects on blood pressure, cardiac output and oxygen consumption, and the fact that oligemia is not the initiating mechanism in at least some types of infectious shock. The occurrence of the latter, whether due to dehydration or loss of plasma or blood, is of serious consequence in infectious shock.

Factors influencing occurrence of infectious shock. The occurrence of severe diarrhea in cholera, bacillary dysentery, ulcerative colitis and so forth may induce such dehydration and contraction of the circulating blood volume that they are of considerable significance in the precipitation of shock. Whether the cardiovascular dynamics in such patients differ from those observed in nonoligemic shock is not known.

Andrews and Harkins⁵¹ measured the weight of pneumonic lungs and concluded that sufficient plasma and blood is lost to account for the occurrence of shock on an oligemic basis. As has been pointed out above, measurements of the circulating blood volume in shock and pneumonia have presented conflicting results. Other examples of rapid loss of plasma in infections are offered by phlegmonous areas and pleural empyema. It should be noted that, although the amount of plasma loss alone may not be sufficient to account for the induction of shock, it is certainly a deleterious factor. In 1920 Lautenschläger⁵² analyzed the effects of the intravenous injection of unconcentrated filtrates of cultures of *Clostridium septicum* and concluded that the circulatory collapse so induced was due to a cardiotoxic digitalis-like effect of the toxin. More recent studies by other investigators have

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

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CASE 31451

PRESENTATION OF CASE

First admission. A fifty-one-year-old man entered the hospital complaining of shortness of breath.

Two years before admission, after lifting a heavy object, he had an attack of severe dyspnea lasting about thirty minutes. Six months before admission he had a similar attack after undue exertion. Four months later sporadic dyspnea on moderate exertion appeared and gradually became severer. Orthopnea and ankle edema developed. Three days before admission he was seized with a severer attack of dyspnea than he had ever had, and it persisted until admission. Orthopnea, insomnia and a nonproductive cough were present. The abdomen increased markedly in size.

At the age of twenty, and again at thirty-five, the patient had complained for several months of migratory joint pains. He had never had substernal pain or oppression.

Physical examination revealed an obese, cyanotic man sitting upright in bed and breathing rapidly and with difficulty. The chest was barrel-shaped, and rales were heard throughout both lungs. Percussion of the heart was unsatisfactory. Over the aortic area and along the left border of the sternum a soft, early diastolic murmur was heard. A soft systolic murmur was heard over the aortic area. The sounds were distant and of poor quality. Fre-

quent extrasystoles were heard, but they were too weak to cause any irregularity of the pulse. The abdomen was greatly distended and tympanitic, but no masses or fluid could be detected. The ankles showed moderate pitting edema. The reflexes were physiologic.

The temperature was 101°F, the pulse 60, and the respirations 35. The blood pressure was 160 systolic, 50 diastolic.

Examination of the blood revealed a red-cell count of 6,300,000, with 91 per cent hemoglobin (Sahli), and a white-cell count of 16,900, with 68 per cent neutrophils. The urine was normal. A blood Hinton test was negative. An x-ray film of the chest showed enlargement of the heart, more pronounced to the left than to the right, with slight tortuosity of the aorta. The hilus vessels were moderately enlarged. There was a poorly defined homogeneous dullness of ground-glass appearance occupying the lower two thirds of the medial portion of both lung fields. An electrocardiogram showed auriculoventricular block (usually 2:1), with occasional sinoauricular block.

Profuse diuresis was obtained after the administration of Mercupurin. The patient was discharged improved on the twentieth hospital day, with instructions to take digitalis.

Second admission (five years later). After discharge he was followed in the Out Patient Department, where it was found that his symptoms of congestive failure had almost completely subsided. The pulse rate was about 50 and irregular. Two years later the patient caught cold and noted increased dyspnea. He wheezed and had a frequent cough. He was slightly cyanotic. The heart rate was 100 and regular. The liver was not enlarged. He improved on digitalis. Three years after this examination, exertional dyspnea again became distressing and the abdomen enlarged. He was readmitted to the hospital.

The blood pressure was 170 systolic, 60 diastolic. Rhonchi and wheezes were heard throughout both lungs. There was dullness at the bases. The heart sounds were distant, the rate was 50 and regular. Aortic systolic and diastolic murmurs were present. The abdomen was distended and tympanitic, with a fluid wave. Ankle edema was present. The blood

infections That produced by physical methods, such as diathermy and hot baths, differs from infectious fever Not only is there no chill phase, but the flush phase is greatly accentuated, since heat dispersal is usually impaired by a warm environment The circulatory changes in physically induced fever are similar to those observed in the flush phase of typhoid-vaccine fever, except that a more marked increase in blood flow through the skin is present in physically induced fever Whereas the blood pressure changes are variable, the peripheral resistance falls The inability of the patient to lose heat normally results in an increased sweating and in extreme hyperventilation Thus, dehydration, decreased blood volume¹⁴ and severe alkalosis may result The extreme hyperventilation may be associated with oxygen unsaturation of the arterial blood⁷⁶ These changes induced by therapy in a patient with a febrile disease have been reported to be associated with the development of shock⁷⁷ The administration of adequate amounts of fluid and, when necessary, oxygen prevents the development of this syndrome

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the left ventricle, and a ground-glass appearance in the central portions of the lung fields, which is quite characteristic of pulmonary edema. A month later the lung fields are clear. The heart remains about the same size.

Four years later the heart was a little larger than it was on the first examination and the hilar shadows were more prominent. An examination within recent months shows the lung fields to be quite clear.

DR. WILLIAMS: Do you think that the heart looks smaller in this last film than it did six years earlier?

DR. SCHULZ: It appears to be, but there may have been a change in technic in the interval. The whole chest appears to be somewhat smaller. Certainly the heart is not larger than it was six years previously.

DR. WILLIAMS: Six years elapsed between the first and the final admissions. During that time the patient did remarkably well, barring an occasional episode of congestive failure. Auricular fibrillation was observed during the third hospital admission and apparently remained the dominant rhythm until death.

At the time of the final admission, there was a sudden increase in the severity of congestive heart failure, perhaps as a result of stopping digitalis or of recurrence of rheumatic infection. A marked precordial thrust was palpable in the left midaxillary line, suggesting the possibility that such cardiac enlargement might have been on a basis of progressive valvular disease. When such enlargement follows generalized involvement of the myocardium, as in acute rheumatic fever or myocardial infarction, the apical thrust is feeble.

The outstanding feature of the final admission was anuria. At first, congestive heart failure seemed sufficient to account for it, but the urine finally passed was bloody. Was this glomerulonephritis or a toxic nephrosis resulting from the use of a mercurial diuretic? It is generally believed that mercurial diuretics do not ordinarily damage the kidney. This, however, is not an ordinary situation. One of the most important factors in toxicity of these drugs is the rate of renal excretion. That was brought out when the use of xanthine derivatives with mercurials was first introduced. It was seen that the mixture produced much more rapid excretion than the mercurial alone and was less toxic in animals. Here a considerable quantity of Mercupurin was held in the body for a long time, and thus may have affected some kidney damage. Glomerulonephritis or pyelonephritis usually turns up unexpectedly at these conferences, and I think that we have to consider the possibility of both, although at no time in the past had there been any indication of significant renal disease.

Did this man have a generalized disease that involved the kidney, such as periarteritis nodosa? Disseminated lupus erythematosus must also be con-

sidered, although the course is too long. I believe that lupus can be discarded almost immediately.

The only diagnosis that might tie the whole thing together, so far as the cardiac picture is concerned, is recurrent active rheumatic fever, with chronic progressive aortic-valve disease — stenosis and regurgitation. Perhaps regurgitation was predominant at first, later becoming secondary to stenosis, at it often does. I should not be too surprised if he had some stenosis of the mitral valve, even though there was no evidence of it in the x-ray films and it was never picked up clinically.

What other etiologic types of heart disease should be considered? Sclerosis of the coronary arteries alone rarely produces congestive failure. Congestive heart failure often follows myocardial infarction, but the electrocardiograms in this case did not suggest infarction at any time. There is a group of destructive myocardial processes falling under the heading of Fiedler's myocarditis. Such patients eventually develop congestive heart failure, but they die after a relatively short time, judging from most of the reported cases of the disease.

DR. GREENE FITZHUGH: Would the fact that no pulsation was detected in the dorsalis pedis arteries indicate a fair amount of vascular disease? Of course, it might have been because the patient was in shock.

DR. WILLIAMS: He was also fibrillating at that time. It is not stated whether the pulsations appeared later.

CLINICAL DIAGNOSIS

Rheumatic and hypertensive heart disease, with congestive failure

DR. WILLIAMS'S DIAGNOSES

Rheumatic heart disease, with aortic stenosis and possibly regurgitation
Recurrent rheumatic fever
Cardiac enlargement
Congestive heart failure
Toxic nephrosis (mercury)
Glomerulonephritis?

ANATOMICAL DIAGNOSES

Acute nephrosis (? Mercupurin)
Acute glomerulonephritis
Cardiac hypertrophy, rheumatic, coronary and hypertensive types

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy showed an extremely large heart, weighing about 800 gm. This man did have systolic hypertension all the time, and I am wondering whether that may have played some role in the hypertrophy, because, as was suggested, the valvular disease was not particularly prominent. There was slight thickening of the

and urine were normal. The nonprotein nitrogen was 34 mg per 100 cc. An x-ray film of the chest showed marked enlargement of the left ventricle and prominent vascular markings. There was no free fluid in either base. An electrocardiogram showed a ventricular rate of 60 per minute, with 2:1 auriculoventricular block, left-axis deviation, depressed ST₁, ST₂, and ST₃, inverted T₁, diphasic T₂, upright T₃, and inverted T₄. He was discharged improved on the fourth hospital day.

Third admission (one year later). The patient was followed in the Out Patient Department and remained in good condition until he cut his left foot while paring a corn. Pain, swelling and redness appeared. He was admitted for treatment of the infection, which subsided rapidly. The blood pressure was 210 systolic, 80 diastolic, and auricular fibrillation was present. The feet were cold, and no dorsalis-pedis pulse was detected. He was discharged on the sixth hospital day.

Final admission (seven months later). After discharge, auricular fibrillation continued. Two weeks before his final admission, at the age of fifty-seven, he returned to the Emergency Ward complaining of an itching red rash starting on the forearms and later spreading to the trunk and legs. Linear rows of vesicles were seen on both arms, with swelling and tightness of the skin, and many crusted lesions. There was an erythematous rash in the axillas and on the trunk and legs. The rash subsided within a week, but the swelling persisted. At about that time the patient discontinued digitalis, and four days later he noted swelling of the legs and orthopnea. The quantity of urine decreased. The blood pressure was 200 systolic, 70 diastolic. He was given 1 cc of Mercupurin intravenously in the Out Patient Department, but he passed only a few drops of urine. Two more cubic centimeters of Mercupurin was administered, but he remained anuric. He was unable to sleep, noted progressively severe dyspnea, orthopnea, swelling of the abdomen and ankle edema and had a loose cough productive of white frothy sputum. There was no hemoptysis, hematuria or pain in the chest or abdomen.

Physical examination revealed an apprehensive, orthopneic and slightly cyanotic man. Dullness and coarse rales were found throughout the lungs. The heart was enlarged about 12 cm. to the left of the midline and 1 cm. to the right of the sternum. A marked precordial thrust was palpable as far laterally as the left midaxillary line. The apical rate was 126, and the radial 63. An aortic systolic murmur was prominent. The skin was tense over a distended abdomen in which shifting dullness could be only questionably demonstrated. The liver was enlarged, being palpable 2 cm. below the right costal margin. There was marked pitting edema of the sacrum and lower legs. The reflexes were sluggish but present.

The temperature was 98°F, and the respirations 25. The blood pressure was 220 systolic, 80 diastolic.

Soon after admission the patient passed about 150 cc of urine, the first in more than forty-eight hours. It was cloudy, amber and acid in reaction, the specific gravity was 1.019. It gave a +++ test for albumin, and the sediment contained about 100 red cells, 20 to 50 white cells and many hyaline and granular casts per high-power field. It was negative for sugar, acetone and bile. The red-cell count was 4,280,000, and the white-cell count 9200, with 69 per cent neutrophils.

The patient remained dyspneic, orthopneic and apprehensive. The pulse rate became regular at 60. An electrocardiogram showed complete heart block, but no sagging of the ST segments. He was treated with morphine, aminophyllin, ammonium chloride and the Schemm diet, but no more Mercupurin was given. Oliguria persisted. He expired on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR CONGER WILLIAMS. The symptoms leading up to the first admission could represent several things, the likeliest being pulmonary congestion secondary to left-sided heart failure brought on by exertion. Another thing that I thought of but discarded was spontaneous pneumothorax, which may be initiated by effort. That diagnosis does not fit in with later events, however.

The migratory joint pains make it seem quite likely that at some time in his career the patient had had active rheumatic fever. When he was first admitted, there may have been some rheumatic scarring of the heart valves, but not enough to account for the heart failure because the only murmurs described at that time were a soft systolic and a slight diastolic murmur, both in the aortic area, which certainly do not indicate significant mechanical defects. Therefore, other possibilities, such as rheumatic activity, must be considered, as well as pulmonary embolism, often a complication in such a situation. Syphilitic aortitis is suggested by the aortic diastolic blow. Heart failure sometimes follows slow complete occlusion of one of the mouths of the coronary arteries in that disease, but the long duration of heart failure here rules out that possibility. Mitral stenosis might also be considered to explain the long-standing pulmonary congestion, in spite of the absence of the characteristic murmur, which is sometimes difficult to hear in an obese patient. It is unusual, however, for mitral stenosis to produce marked peripheral congestion in the absence of auricular fibrillation except in the course of active rheumatic infection.

May we see the x-ray films?

DR MILFORD D SCHULZ. These films cover a period of six years. The first shows a heart apparently enlarged in all diameters, principally in

The temperature was 99°F, the pulse 110, and the respirations 25. The blood pressure was 160 systolic, 75 diastolic.

Examination of the blood revealed a red-cell count of 5,100,000, with 12.5 gm of hemoglobin, and a white-cell count of 3900. The urine gave a +++ test for albumin. The sputum was yellowish and negative for acid-fast bacilli. A moderate number of Type 3 pneumococci were found on culture of the sputum. The nonprotein nitrogen was 86 mg per 100 cc.

An x-ray film of the chest taken the day of admission showed the left lung to be clear. In the right lung there was a hazy, flecky area of increased density in the central portion, with continuous areas of increased density in the lower lung field. There was no evidence of pleural fluid. The heart was prominent in the region of the left ventricle, and the aorta was tortuous. A film taken three days later showed the process to be chiefly in the right middle lobe, with some changes in the lower lobe. The general appearance was that of an extensive peribronchial process involving the middle and lower lobes.

During the patient's hospital course, the temperature varied from 98 to 100°F, rising on one occasion (three days before death) to 104°F. During the first two days his condition was good. On the fifth hospital day, however, his respirations increased to 58 per minute and he had shaking chills. The skin was hot and moist. The lower half of the right lung posteriorly was dull to percussion, with bronchial breathing in this area. Penicillin was begun, 16,000 units being given every two hours. There was no evidence of cardiac failure. The following day the temperature was 98.8°F, and the respirations were slower and less labored. Dullness and bronchial breathing persisted in the lower portion of the right lung. One day later, severe dyspnea again appeared and both lungs were full of coarse bubbling rales. The patient expired on the eighth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. ARTHUR J. LINENTHAL: I should like to inquire whether the urinary sediment was examined and whether blood cultures were taken. If so, what did they show?

DR. RONALD C. SNIFFEN: The urinary sediment is not reported, and no blood cultures were taken.

DR. LINENTHAL: We have an eighty-six-year-old man who came in complaining of cough and blood-streaked sputum for one month, both of which seem to point to some pulmonary process. I think that it is impossible in this case to find one diagnosis that will explain all the abnormalities this man had, and I shall first mention several things that I believe cannot be included in the primary diagnosis.

It is interesting that this man was apparently in good general condition. He was well developed and

well nourished, and during the first two or three hospital days his condition was thought to be good. This must have been true, because apparently no specific therapy was started. He had some skin lesions on his back, which were possibly associated with uremia, a condition that sometimes produces skin lesions. They might have been related to drugs taken before admission, or they might have been due to pressure, since I assume that this patient was probably in bed for a short time before he came to the hospital. The excoriated lesions on the hand are not significant, they were probably senile keratoses.

The patient had hypertension on admission, and the blood pressure might well have been higher previously. Probably associated with hypertension, he had cardiac enlargement, demonstrable both by physical and by x-ray examination. He had a systolic murmur at the apex that could well have been the systolic murmur of functional mitral regurgitation associated with left ventricular enlargement, as part of what we might call the cardiac picture. He had bilateral ankle edema, we are not told whether it was pitting. The serum protein level is not given. A low serum albumin might have been of interest in a patient with albuminuria. The dyspnea might also have been related to the cardiac enlargement, although of course it could have been due to the pulmonary factor. It seems as though he might well have had a mild degree of congestive heart failure.

He also had a +++ albuminuria, an elevated nonprotein nitrogen and slight anemia, which point toward some renal lesion, and in a patient of this age it seems likeliest that he had a chronic arteriolar nephrosclerosis. The description of the yellowish red urine for several months before he came to the hospital is interesting but impossible to evaluate. He had had some nocturia, which is not too surprising in a patient of this age, and it could have been related to the mild cardiac failure, to renal failure or to benign prostatic hypertrophy.

We then come to the pulmonary picture, which was the presenting problem, the cough, sputum, hemoptysis and dyspnea all pointing to a lesion of the lungs. Physical examination showed some abnormality, and x-ray examination revealed a rather extensive process.

May we see the x-ray films?

DR. CLAYTON H. HALE: These films show the uniform process described. We see the linear markings, described as peribronchial extension, throughout the greater portion of the right lung field. There is some increased density in the lower lobe. The shadow of the diaphragm is fairly well obscured posteriorly. I think that one also has to say that there is definite abnormality in the upper lobe. There is no significant amount of fluid in the chest. If this is pulmonary edema, it is not on a cardiac basis, since I cannot make out any enlargement of

mitral valve, and slight interadherence of the aortic cusps. The amount of stenosis in these valves was slight, but they probably did contribute to the heart failure, because we found no other cause for enlargement of the heart.

DR WILLIAMS: Did you find any evidence of old rheumatic myocarditis or anything of that sort?

DR CASTLEMAN: No, not in the sections that we have seen.

DR WILLIAMS: How about the coronary arteries?

DR CASTLEMAN: They showed severe sclerosis, but we did not find any evidence of old infarction. They were extremely narrow.

The striking finding in the case was in the kidneys. Together they weighed 800 gm., which is almost three times the normal weight. They were markedly swollen, red and mottled, and on section there was no clear line of demarcation between the cortex and the medulla. Microscopically, every glomerular tuft was completely packed with polymorphonuclear leukocytes and almost all the capillary loops were occluded, in other words, they showed the characteristic findings of acute glomerulonephritis. In a few areas we were able to find beginning proliferation of the capillary endothelium of the glomeruli, indicating that the process had been going on for several weeks. I do not know whether or not it antedated that period, but certainly the duration was no longer than a month or six weeks. Most of the convoluted tubules showed epithelial degeneration. This was much more than a mere cloudy swelling, it was a true nephrosis. There were also fat granules within some of the epithelial cells and within the lumen. Several of the tubules already showed evidence of regeneration and repair. We know that repair can occur within three or four days after the onset of necrosis, so that we have evidence here of some injurious agent that had attacked the tubules quite recently. Of course, in this particular case we should like to incriminate Mercupurin, and indeed, I do not see how it can be avoided. When he came to the Emergency Ward five days before admission to the hospital, he complained of edema and said that he had stopped taking digitalis, at that time he was given 1 cc of Mercupurin. If we assume that he had a glomerulonephritis at that time, it is possible that the Mercupurin was enough to injure the tubules to this extent. He died five or six days later, which would give enough time for the repair process to have begun. I believe that this is the first case that we have ever had in which there has been as much suggestive evidence of injury to the kidneys by Mercupurin.

I looked up the subject two months ago, not extensively, to be sure, and in the only two cases that I could find the patient had also been given bismuth for syphilis, so that no conclusions were possible.

DR JOSEPH GARDELLA: This man had a severe case of poison-ivy dermatitis and was given sub-

cutaneous injections of material made up by his local doctor. It came in a vial, was mixed in a glass and pounded for a while and was then injected.

DR CASTLEMAN: Do you mean that this material might have been the toxic agent rather than the Mercupurin?

DR GARDELLA: He received no diuretic effect from Mercupurin, but it did not seem to make him particularly worse.

DR FITZHUGH: Did you not say that the glomerular damage was of several weeks' duration?

DR CASTLEMAN: That was a different process. It was not due to Mercupurin, just a straight glomerulonephritis, which can occur even in a person of eighty. That is the reason why I believe that the Mercupurin might have been an added insult to a previously injured kidney, but as Dr Gardella has just brought out, it is quite possible that whatever he received for the poison-ivy rash might have been the causative factor.

DR WILLIAMS: Do you ever see this histologic picture in the course of glomerulonephritis?

DR CASTLEMAN: Not so severe as this. The kidneys usually do not weigh so much. I was puzzled by this combination of processes and showed the slides to Dr Frederic Parker, Jr., at the Boston City Hospital, asking him whether it was possible to get this picture in straight glomerulonephritis. He said that he had never seen it. He thought that the reparative changes in the tubules were fairly good proof that there was a toxic agent in addition to the nephritis.

CASE 31452

PRESENTATION OF CASE

An eighty-six-year-old man entered the hospital complaining of a chronic cough.

The cough, which was of a month's duration, was productive of tenacious white sputum and occasionally blood streaked. During this period he had also noticed increasing dyspnea, as well as swelling of the right ankle. He had had occasional chills and fever, the last episode occurring one week before admission. The urine had been yellowish red for several months, he had nocturia. The past history was non-contributory.

Physical examination revealed a well developed and well nourished man in no distress. A diffuse maculopapular eruption was seen over the back, and there were a few excoriated lesions on the dorsum of each hand. The tongue was dry and furrowed. The point of maximum cardiac impulse was in the fifth interspace 10.5 cm. to the left of the midline. A systolic murmur was heard at the apex. Over the right lung base there was flatness, with decreased fremitus and rales. There was bilateral ankle edema, more marked on the right than on the left. The reflexes were physiologic.

led him. It is good geriatrics to get him up as soon as possible and let him do about as he pleases." Shortly after that the service changed, and apparently he stayed in bed and died. I wonder if they had gotten him up whether he would still be with us.

DR. W. WILSON SCHIER The terminal episode suggests pulmonary embolism — the high respiratory rate, the fever and the low white-cell count.

DR. LINENTHAL I mentioned the possibility of pulmonary infarction to explain the terminal episode. It could also have been due to a massive pulmonary embolism without infarction.

DR. WADE VOLWILER I remember this man because his case taught a valuable lesson to the house staff. In the first place, because of the emphasis that he continually placed on the blood-streaking of the sputum, which occurred daily and began with the onset of the productive cough, we thought that he must have a neoplasm of the lung as the basis of his difficulties. We also believed that he had a certain amount of secondary infection behind the process.

The cough was extremely productive.

He was a well preserved, agile man of eighty-six and was kept out of bed as much as possible, even after Dr. Means left the service. The immediate problem arose whether we should investigate the process further by means of bronchoscopy and other such procedures. Because of his age, a severe cervical hypertrophic arthritis and our inability to do much about an extensive carcinoma if we did find it, we elected not to do a bronchoscopy. We did decide, however, to give him one course of penicillin therapy to relieve any secondary infection that might have been present, but this was not done until the morning of the day on which he had the shaking chill and rapid respirations. He then went downhill rapidly and died in coma.

I believe that the elevated nonprotein nitrogen was found in a blood specimen taken in the terminal days, at which time he was quite dehydrated. At no time did we believe that he had signs of cardiac failure: there was little cyanosis, the neck veins were not distended and did not pulsate, there was no gallop rhythm, and the pulse generally was regular.

CLINICAL DIAGNOSIS

Pneumonia?
Carcinoma of right lung?

DR. LINENTHAL'S DIAGNOSES

Subacute pulmonary infection (Type 3 pneumococcus)
Hypertensive cardiovascular disease
Nephrosclerosis

ANATOMICAL DIAGNOSES

Bronchopneumonia, bilateral
Chronic bronchitis
Pleuritis, acute fibrinous, left
Nephrosclerosis, slight.
Cerebral infarcts, old

PATHOLOGICAL DISCUSSION

DR. SNIFFEN The important findings at autopsy were confined to the chest. The right pleural cavity merely showed fibrous apical adhesions. The left cavity was entirely obliterated by old fibrous adhesions and more recent fibrinous adhesions. The lungs were three to four times their normal weight — 2250 gm. Throughout the entire left lung and in the right upper and lower lobes there were large patchy areas of gray consolidation, the right middle lobe was edematous. The heart weighed 440 gm., a little above the upper limit of normal, but was essentially negative, apart from a mild coronary atherosclerosis. A blood culture was sterile.

Microscopically, sections of the lungs showed an extensive and severe bronchopneumonia, and judging from the condition and quality of the exudate, it seemed to be of approximately one week's duration. The bronchi, on the other hand, showed chronic changes, in that there were fibroblastic proliferation in the walls, slight epithelial metaplasia and a few partially organized fibrinous plugs in the lumens. The kidneys showed a mild nephrosclerosis and a suggestion of pyelonephritis.

DR. MEANS What was the state of the aorta?

DR. SNIFFEN Remarkably free of atheromatous change.

DR. MEANS Dr. Albright is always quoting the late Dr. Erdheim as saying that if one lives to be over eighty, one must have a smooth aorta, because if one does not have a smooth aorta, one does not live to be over eighty. We do not get autopsies often on octogenarians. It might be worth while to call your attention to an interesting clinicopathologic conference by Dr. Holyoke, of Salem. He lived to be over one hundred years old and made an anatomical diagnosis on himself. He requested that all the doctors in Salem be invited to see his autopsy. Most of them came. It was stated that the aorta was just as smooth as a youth's and that the heart was absolutely normal, indeed on the small side. An autopsy on anyone over eighty is of interest from that angle. The present one seems to bear out Dr. Erdheim's statement, although I recall one patient over eighty who had a rough aorta, so the maxim does not always hold.

DR. CHARLES S. KUBIK The pathology in the brain contributed nothing to the symptomatology described here. There were a number of small infarcts, the larger ones being in apparently silent areas in the frontal and occipital regions.

the vascular shadow on the left. We must also consider metastatic malignancy in the right lung, possibly with superimposed pulmonary edema. The findings could also be due to diffuse areas of consolidation on an infectious basis.

DR JOSEPH AUB: Is there any collapse of the right lower lobe?

DR HALE: I do not believe so, although it may be a little smaller than normal. At least it is not aerated, which suggests fluid or consolidation.

DR LINENTHAL: In discussing the pulmonary process there are several types of conditions that one must consider—infection, carcinoma and, as Dr Hale suggests, pulmonary edema, or possibly a combination of two of these three possibilities. It is important to know that apparently there was no past history of pulmonary symptoms.

So far as infection is concerned, the bouts of fever and chills that this man had are consistent with an infectious process, due either to a primary infection or to a neoplasm with secondary areas of necrosis or infection. We are given a clue in the laboratory examinations to one specific bacterial agent, namely, a Type 3 pneumococcus, which grew in moderate amounts in a culture of the sputum. The picture certainly was not that which we are accustomed to see in the majority of people with pneumococcal pneumonia: there was no acute onset, the patient was not acutely ill and had no chest pain, and he had no fever except during the episode of chills. Furthermore, the duration was rather long for a pneumococcal pneumonia. In an eighty-six-year-old man, however, pneumococcal infection can behave peculiarly, and one may find a pathologic process that is entirely out of proportion to the general condition of the patient, in other words, the general condition of the patient may continue to be quite good in spite of the fact that the pathologic process is extensive. The normal white-cell count is interesting, and I suppose that it represents the inability of this old man to respond to an infection in the lungs, just as does the absence of any striking continued fever. The Type 3 pneumococcus is a rather frequent organism in the normal upper respiratory tract, and this fact makes the situation a bit confusing. It is also, however, one of the types of pneumococci usually found in older people, and probably because of this the pneumonia that it produces has a higher mortality rate than those caused by other types.

Another possibility that one thinks of in passing is tuberculosis. It seems unlikely on the basis of the patient's age and on the basis of the x-ray picture, and at least one examination of the sputum was negative for acid-fast organisms.

The question of atypical or so-called "virus" pneumonia should be mentioned, but there seems to be little in the picture to make one think too strongly of that. One might also think of a chronic or perhaps subacute nonspecific bacterial inflam-

matory process in the lung, so-called "chronic pneumonitis." There is no history of a pre-existing underlying pulmonary lesion on which this might have been superimposed, but the patient was an old man and he had uremia, both of which might have increased his susceptibility to infection. The chills and fever would also be consistent with chronic pneumonitis.

Did this man have a carcinoma of the lung? As Dr Hale mentioned, the x-ray picture may be that of metastatic disease. There is nothing to indicate a primary tumor elsewhere. The urinary tract is suspect, but I think that the findings can be explained on the basis of hypertensive disease. The development of symptoms, beginning with cough and blood-streaking rather than with gross hemoptysis, and the chills and fever are consistent with pulmonary carcinoma. The duration is rather short but is possibly accounted for by a superimposed infection on a carcinoma that had been silent for a time previous to the onset of symptoms. The x-ray lesion is rather extensive for a primary neoplasm of the lung, involving as it probably does all three lobes, with the major process in the right middle lobe. Certainly if he did have carcinoma, he must have had a rather extensive superimposed infection.

In the hospital he had an episode of rapid respiration and dyspnea, which was probably associated with the chills and fever, and it seems that this was similar to the previous episodes of chills and fever. The next day, the temperature came down to normal and he was apparently much better. The record states that he had no evidence of cardiac failure at that time. I assume that this probably means that the lungs were not full of bubbling rales. Penicillin was begun at that time. The patient was better the next day, but I see no reason to believe that the improvement was due to the penicillin.

The terminal episode, which followed two days later, was apparently one of acute pulmonary edema. This could well have represented an extension of the pulmonary infection, or it might even have been associated with a massive myocardial or pulmonary infarction.

In summary, I think that this man had a subacute pulmonary infection, probably due to a Type 3 pneumococcus. I believe that a neoplasm of the lung is unlikely. In addition, I believe that he had hypertensive cardiovascular disease and marked nephrosclerosis, which caused nitrogen retention and cardiac enlargement.

DR AUB: Would Dr Linenthal consider a primary tumor of the kidney—a hypernephroma or renal-cell tumor?

DR LINENTHAL: It is possible. On the basis of the evidence we have, I do not see how one could go any farther than to raise the question.

DR J. H. MEANS: I saw this man and wrote the following note: "The patient is an eighty-six-year-old man and rapidly recovering from whatever

horacic, gastrointestinal, spinographic and foreign-body examinations. The fact that it is time consuming and requires special skill should be no excuse for failure to use fluoroscopy in modern radiologic practice.

Those who were responsible for these early advances had an excellent clinical background, a sound knowledge of the basic sciences and an investigative mind. Little insight is needed to recognize that this is as true now as it was then.

The second chapter of this era was one of consolidation and comprised establishing standards for good radiologic practice and making them possible by a well planned training program. The medical profession had recognized radiology as a full-fledged specialty. In 1924 the American College of Radiology was founded for the purpose of studying and correlating the educational and economic aspects of radiology, to advance this science and to improve its services. In 1934, the three American radiologic societies, the College of Radiology and the Section on Radiology of the American Medical Association recognized the necessity for establishing high minimum requirements for physicians practicing this specialty. They founded the American Board of Radiology, with an examining panel to certify diplomates in five categories according to the training and experience of the applicant: radiology (the practice of the entire specialty), roentgenology (excluding the practice of radium therapy), diagnostic roentgenography (excluding all therapy), therapeutic roentgenology (excluding diagnostic practice), and radium therapy. The applicant must hold himself out to be a specialist in radiology or one of its branches and must have the following minimum training requirements: a graduate of a Class-A medical school, a one-year internship in an approved hospital, and a three-year residency in radiology, including six months of applied pathology and a grounding in the basic sciences and the theories of radiation. In addition, an examination by the Board must be passed for certification. Statistics show that one out of every three applicants fails.

As a corollary to the above requirements, a training program for radiologists had to be initiated. The American Board of Radiology, in co-operation

with the Council on Medical Education and Hospitals of the American Medical Association, has helped establish standardized residencies in American teaching hospitals to satisfy the demand for well trained radiologists. There are over one hundred such residencies available at present, and every effort is being made to increase this number so that any qualified returned medical officer who desires to follow the specialty can be trained.

The next chapter lies in the future. Adequate tools and technics are available. The specialty has established high standards and an educational program to meet them. In the next few years enough well trained radiologists will be on hand to offer modern radiologic services to both large and small hospitals and to private practice as well. The future of radiology is closely integrated with the future of medicine as a whole. Progress depends more than ever on the true co-operative spirit among the various branches of medicine, pooling individual skills and knowledge. It is no longer good medicine to be a "lone wolf" in handling problem cases.

The duty of the radiologist is not to confirm the clinical impression but to give a radiologic consultation, which, when added to the clinical and laboratory data, will lead to a correct diagnosis. Therefore, he must have at hand pertinent data concerning the patient at the time of the examination. It is hoped that the return of doctors from the armed services will allow the physician of tomorrow enough leisure to make use of the opportunity for consultation and discussion, which were not possible in the rushed wartime years. It is through the medium of this exchange of ideas that medicine will advance with the same strides that it has in the past.

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FIFTIETH ANNIVERSARY OF THE DISCOVERY OF X-RAYS

Just fifty years ago today, November 8, 1895, a new epoch in medicine was opened with the discovery of the x-ray by Wilhelm Conrad Roentgen. Although the ray has been officially designated the "roentgen ray" in his honor, the more convenient name Roentgen first employed, "x-ray," is generally used. Roentgen not only discovered the x-ray and described its properties, but he also observed that this ray would penetrate certain opaque objects, among them the human body. The medical world was quick to perceive the great diagnostic and therapeutic possibilities of this ray. Nearly all the

organs of the body are now accessible for study, either directly or indirectly. Carefully controlled voltages from 20,000 to 3,000,000 are available for therapeutic work alone or in conjunction with radium. Lately, the armamentarium has been increased by artificially produced radioactive substances, some for internal use, the application of which is being explored.

The first chapter of the x-ray era was written by keen clinicians employing this new modality as an aid toward better diagnosis. These pioneers made good use of their knowledge of anatomy, physiology and pathology to discover methods of examination and treatment. Progress since then has been a race between the development of more powerful and more versatile apparatus and its adaptation to the fields of diagnosis and treatment.

Lest the young enthusiast be inclined to rest on his laurels, a review of the first decade of x-ray progress will bring with it a humble frame of mind. It is amazing that the early investigator who unknowingly risked his life with the crudest of makeshift equipment produced so much. Between the years 1895 and 1901, Francis H. Williams, William Rollins and Walter B. Cannon, to mention just a few, outlined many of the fundamental diagnostic and therapeutic criteria used today. It was Williams who threw a bombshell into a meeting of a medical society by maintaining that he could discover pulmonary tuberculosis by this new method earlier than by auscultation and percussion. In 1901 Williams's reports of cases treated by x-ray would put many modern physicians to shame because of their completeness—a good history and description of the lesion, a biopsy done by Frank B. Mallory, detailed data of the technic used, extensive progress notes and photographs taken before and after treatment to document his results.

The importance of the fluoroscopic examination was emphasized by Williams, Crane, Rieder, Carmen and others from the inception of the specialty. It was one of the earliest tools, and only through the fluoroscope can the living dynamic aspects of anatomy, physiology and pathology be studied. Roentgenoscopy and roentgenography should be considered and used as complementary procedures for

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PENICILLIN BLOOD LEVELS FOR TWENTY-FOUR HOURS FOLLOWING A SINGLE INTRAMUSCULAR INJECTION OF CALCIUM PENICILLIN IN BEESWAX AND PEANUT OIL*

CAPTAIN MONROE J. ROMANSKY, M C, A U S, AND
TECHNICIAN (3RD GRADE) GEORGE E. RITTMAN, M DEPT, A U S

IN PREVIOUS reports, we¹⁻³ have shown that after a single injection of a suspension of calcium penicillin in beeswax and peanut oil, effective levels of penicillin can be maintained in the blood for ten to twelve hours, with excretion continuing in the urine for twenty-four to thirty-two hours. Clinical results^{3, 4} have proved as satisfactory by this method of administration as by the method utilizing penicillin in saline solution, which necessitates multiple injections. The preparation most satisfactory for obtaining the above results has proved to be a suspension of 100,000 units of calcium penicillin in 4 per cent beeswax by volume (3.2 per cent by weight) in peanut oil contained in 1 cc. The actual weight of beeswax obtained from a pipette containing 1 cc is 0.8 gm. Thus, 4 per cent by volume is equivalent to 3.2 per cent by weight.

Our objective has been to prepare a mixture of penicillin that after a single injection will maintain adequate levels of penicillin in the blood for at least twenty-four hours. It was stated in a previous paper² that the factor limiting the amount of penicillin that can be suspended in 1 cc of beeswax and peanut oil is the potency, in Oxford units per milligram, of the penicillin. Early mixtures, which were handshaken, had 30,000 to 50,000 Oxford units of calcium penicillin in beeswax and peanut oil, contained in 1 cc. Since the calcium penicillin averaged 200 to 250 Oxford units per milligram, in terms of amount by weight, the mixture contained approximately 250 mg in 1 cc.

Subsequently, with the use of a mechanical blender, the particles of penicillin were broken down more finely by agitating the dry powder. The beeswax peanut oil was then added to the powder, and the mixture was blended mechanically. Simultaneously, calcium penicillin assaying at 300 to 500 Oxford units per milligram was available.

It was found at this time that the maximum quantity of penicillin powder that could be suspended in beeswax and peanut oil and still be satisfactory from the standpoint of viscosity and prolonged action was approximately 300 mg contained in 1 cc. This quantity of penicillin displaces about 0.2 cc of the beeswax and peanut oil in the final suspension. Therefore, in the preparation of the material, 0.8 cc of beeswax and peanut oil is added so that the final mixture is contained in a volume of 1 cc. With a potency of 300 to 400 units of calcium penicillin per milligram, satisfactory mixtures of 100,000 units (250 to 300 mg) of penicillin in 4 per cent beeswax by volume (3.2 per cent by weight) in peanut oil were obtained, with the results shown previously.³

It had been hoped that by increasing the volume of a given amount of penicillin per cubic centimeter, a more prolonged effect might be obtained. It was demonstrated, however, that, although 100,000 units in 1 cc gave a satisfactory assayable level in the blood for an average of seven and a half hours, increasing the total to 3 cc or 300,000 units resulted in assayable penicillin in the blood for only twelve to fourteen hours. Figure 1 shows the levels of penicillin obtained in the blood after the injection of 100,000, 200,000 and 300,000 units of penicillin in 4 per cent beeswax by volume in peanut oil contained in 1, 2 and 3 cc, respectively. It also shows the duration of excretion of penicillin in the urine with these quantities.

It became obvious that a relatively constant amount of penicillin was being absorbed from each cubic centimeter of the penicillin in beeswax and peanut oil, and by increasing the number of cubic centimeters only slight additional prolongation was achieved, although a marked increase in the height of the level of penicillin in the blood occurred.

When calcium penicillin with a potency of 600 to 800 Oxford units per milligram was obtained, it was possible to suspend 200,000 units of penicillin in 4 per cent beeswax by weight in peanut oil contained in 1 cc. By weight this also represented 250

*From the Penicillin Section, Laboratory Service, Walter Reed General Hospital, Washington, D C.

Miss Dorothy Talbott, Technician (4th Grade) Mina Levy, Miss Lillian Aelrod and Mrs. Mary Ann Gallagher rendered valuable technical assistance in this study.

MISCELLANY

FEDERAL PUBLIC-HEALTH ADMINISTRATION

The Association of State and Territorial Health Officers has recently expressed cognizance of the need of co-ordination, under a single head, of the civilian health activities of the federal government. The several states and territories have been receiving grants-in-aid from both the United States Public Health Service and the Children's Bureau of the Department of Labor for their public-health programs. Originally these grants were made under the Social Security Act, but more recently the grants from the United States Public Health Service have been made under the recodification of the laws pertaining to the public health, known as Public Law 410 of the Seventy-Eighth Congress.

At the present time the several states are required to make reports to both agencies, present their budgets and conform with a variety of regulations issued by these two agencies. In an endeavor to reduce the number of different reports required and to co-ordinate the directives coming from the various federal health agencies, it is the recommendation of the Association that, in the reorganization of the Government, as is being planned by President Truman, serious consideration be given to the establishment of a department of public health with a cabinet officer in charge. It is further recommended that permanent career men be selected for the key positions in this department and that they be given an opportunity to retain their positions on a permanent basis.

The Association has learned that a proposal may have been made for the organization of a department of public health and welfare with a cabinet officer at its head. If this organization is carried through, the Association suggests that adequate measures be taken to ensure that public health receives sufficient freedom of action to carry on its important function of maintaining optimal health for all the people. It is further suggested that, if such a combined department is formed, permanent career undersecretaries or assistant secretaries should be in charge of the two activities and that they should be of equal rank. The Association believes that such a department would be less desirable than a separate department of public health.

These recommendations were made, the Association states, in the interest of better public-health administration on a federal level and of the co-ordination of all civilian public-health activities in a single department, thereby rendering liaison and co-operation with the several states and territories the more efficient and effective. This, in turn, would bring about an improvement in general public-health work throughout the entire country and enable such a department to administer any future legislation pertaining to public health with greater efficacy and with a smaller administrative overhead for services rendered.

NOTICES

ANNOUNCEMENT

Dr A. Louis Hermanson has resumed the practice of surgery at 371 Commonwealth Avenue, Boston.

Dr Antonio P. Milone, who has been discharged from the armed services, will resume practice at 4354 Washington Street, Roslindale, on November 15.

Dr Arnold L. Segel announces the opening of his office at 475 Commonwealth Avenue, Boston, for the practice of general surgery.

SUFFOLK DISTRICT MEDICAL SOCIETY

The fall dinner of the Suffolk District Medical Society will be held at the Harvard Club of Boston on Saturday, November 17. Guests will assemble at 6:00 p.m., and dinner will be served promptly at 7:00 p.m. The speaker will be Brigadier General Elliott C. Cutler, M.C., A.U.S., whose subject will be "Experiences in the European Theater of Operations."

This is to be a "home-coming meeting," and all members of the district society are urged to bring as their guests men

who have been recently discharged from service or those who are still in uniform, the latter will be admitted without charge, regardless of whether or not they are members of the Massachusetts Medical Society. In addition, the members of other district societies are urged to attend. Tickets may be purchased from the treasurer, Dr. Richard S. Everts, 319 Longwood Avenue, Boston 15. Contrary to the custom adopted for the past several years, wives of members will not be admitted.

EXHIBITION AT BOSTON MEDICAL LIBRARY

In commemoration of the fiftieth anniversary of the discovery of the x-rays by Konrad Roentgen, the Boston Medical Library has displayed in the showcases in the rotunda the original papers of Roentgen, together with other material on the history of radiology.

AMERICAN ASSOCIATION ON MENTAL DEFICIENCY

The sixty-ninth annual meeting of the American Association on Mental Deficiency will be held at the Hotel Cleveland, Cleveland, on November 28, 29 and 30 and December 1. The program, as arranged, presents sections on institutional administration, research, psychiatry and medicine in the field of mental defect, psychology and teacher training.

NEW ENGLAND ROENTGEN RAY SOCIETY

The next meeting of the New England Roentgen Ray Society will be held at the Harvard Club of Boston on Friday, November 16, at 8:00 p.m. The fiftieth anniversary of the discovery of x-rays will be commemorated by a special program consisting of the following:

- The Use of X-rays in Art Dr. William J. Elliott
 - Some Industrial Applications of X-rays Dr. Paul E. Tivnan
 - The Application of X-rays to Crime Detection Dr. Joseph T. Walker
 - X-rays as a Tool of the Physician Dr. Bertram E. Warren
 - X-rays in Medicine Dr. Merrill C. Sosman
- Interested physicians are invited to attend.

SUFFOLK CENSORS' MEETING

The Censors of the Suffolk District Medical Society will meet for the examination of candidates at the Boston Medical Library, 8 Fenway, on Thursday, December 6, 1945, at 4:00 p.m.

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, November 20, at 8:15 p.m. Drs. Chester S. Keefer, Max Finland and Charles A. Janeway will present a symposium on recent advances in chemotherapy.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, NOVEMBER 15

FRIDAY, NOVEMBER 16

- *9:00-10:00 a.m. Deep Phlebitis and Pulmonary Embolus Dr. Jacob A. Fine. Joseph H. Pratt Diagnostic Hospital
- *9:00-10:00 a.m. Medical clinic. Isolation Amphitheater Children's Hospital
- 10:50 a.m. Acrodermatitis Related to Vascular Diseases Dr. Eugene E. O'Neil (Postgraduate clinic in dermatology and syphilology) Amphitheater Dowling Building Boston City Hospital
- *8:00 p.m. New England Roentgen Ray Society Harvard Club of Boston

SATURDAY, NOVEMBER 17

- *10:00 a.m.-12:00 m. Medical staff rounds Peter Bent Brigham Hospital

(Notices continued on page x-ii)

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PENICILLIN BLOOD LEVELS FOR TWENTY-FOUR HOURS FOLLOWING A SINGLE INTRAMUSCULAR INJECTION OF CALCIUM PENICILLIN IN BEESWAX AND PEANUT OIL*

CAPTAIN MONROE J. ROMANSKY, M.C., A.U.S., AND
TECHNICIAN (3RD GRADE) GEORGE E. RITTMAN, M.D., A.U.S.

IN PREVIOUS reports, we¹⁻³ have shown that after a single injection of a suspension of calcium penicillin in beeswax and peanut oil, effective levels of penicillin can be maintained in the blood for ten to twelve hours, with excretion continuing in the urine for twenty-four to thirty-two hours. Clinical results^{3, 4} have proved as satisfactory by this method of administration as by the method utilizing penicillin in saline solution, which necessitates multiple injections. The preparation most satisfactory for obtaining the above results has proved to be a suspension of 100,000 units of calcium penicillin in 4 per cent beeswax by volume (3.2 per cent by weight) in peanut oil contained in 1 cc. The actual weight of beeswax obtained from a pipette containing 1 cc is 0.8 gm. Thus, 4 per cent by volume is equivalent to 3.2 per cent by weight.

Our objective has been to prepare a mixture of penicillin that after a single injection will maintain adequate levels of penicillin in the blood for at least twenty-four hours. It was stated in a previous paper² that the factor limiting the amount of penicillin that can be suspended in 1 cc of beeswax and peanut oil is the potency, in Oxford units per milligram, of the penicillin. Early mixtures, which were handshaken, had 30,000 to 50,000 Oxford units of calcium penicillin in beeswax and peanut oil, contained in 1 cc. Since the calcium penicillin averaged 200 to 250 Oxford units per milligram, in terms of amount by weight, the mixture contained approximately 250 mg in 1 cc.

Subsequently, with the use of a mechanical blender, the particles of penicillin were broken down more finely by agitating the dry powder. The beeswax peanut oil was then added to the powder, and the mixture was blended mechanically. Simultaneously, calcium penicillin assaying at 300 to 500 Oxford units per milligram was available

It was found at this time that the maximum quantity of penicillin powder that could be suspended in beeswax and peanut oil and still be satisfactory from the standpoint of viscosity and prolonged action was approximately 300 mg contained in 1 cc. This quantity of penicillin displaces about 0.2 cc of the beeswax and peanut oil in the final suspension. Therefore, in the preparation of the material, 0.8 cc of beeswax and peanut oil is added, so that the final mixture is contained in a volume of 1 cc. With a potency of 300 to 400 units of calcium penicillin per milligram, satisfactory mixtures of 100,000 units (250 to 300 mg) of penicillin in 4 per cent beeswax by volume (3.2 per cent by weight) in peanut oil were obtained, with the results shown previously.²

It had been hoped that by increasing the volume of a given amount of penicillin per cubic centimeter, a more prolonged effect might be obtained. It was demonstrated, however, that, although 100,000 units in 1 cc gave a satisfactory assayable level in the blood for an average of seven and a half hours, increasing the total to 3 cc or 300,000 units resulted in assayable penicillin in the blood for only twelve to fourteen hours. Figure 1 shows the levels of penicillin obtained in the blood after the injection of 100,000, 200,000 and 300,000 units of penicillin in 4 per cent beeswax by volume in peanut oil contained in 1, 2 and 3 cc, respectively. It also shows the duration of excretion of penicillin in the urine with these quantities.

It became obvious that a relatively constant amount of penicillin was being absorbed from each cubic centimeter of the penicillin in beeswax and peanut oil, and by increasing the number of cubic centimeters only slight additional prolongation was achieved, although a marked increase in the height of the level of penicillin in the blood occurred.

When calcium penicillin with a potency of 600 to 800 Oxford units per milligram was obtained, it was possible to suspend 200,000 units of penicillin in 4 per cent beeswax by weight in peanut oil contained in 1 cc. By weight this also represented 250

*From the Penicillin Section, Laboratory Service, Walter Reed General Hospital, Washington, D.C.

Miss Dorothy Talbott, Technician (4th Grade), Miss Levy, Miss Lillian Axelrod, and Mrs. Mary Ann Gallagher rendered valuable technical assistance in this study.

tion of penicillin occurs from 1 cc of these mixtures. If the concentration is increased in 1 cc, a prolongation of the blood level and excretion results.

As a rule, proportionate amounts of the 300,000

units in 1 cc is given for eight days, penicillin continues to be excreted in the urine for approximately six days following the last injection, as compared

TABLE 1 *Penicillin Blood Levels Produced by a Single Intramuscular Injection of 300,000 Units of Calcium Penicillin in 4.8 Per Cent Beeswax by Weight in Peanut Oil Contained in 1 cc*

CASE No.	TIME AFTER INJECTION							DURATION OF ASSAYABLE LEVEL (0.039 UNITS PER CC.)
	½ hr.	4 hr.	8 hr.	12 hr.	16 hr.	20 hr.	24 hr.	
	units/cc	units/cc	units/cc	units/cc	units/cc	units/cc	units/cc	hr.
1	0.156	0.625	0.625	0.312	0.156	0.078	0.078	24
2	0.312	0.156	0.078	0.156	0.078	0.156	0.156	24
3	0.625	2.50	0.312	0.312	0.156	0.039	0.039	24
4	1.25	1.25	1.25	0.078	0.078	0.078	0.078	24
5	1.25	1.25	0.625	0.625	0.156	0.078	0.078	24
6	0.625	1.25	1.25	0.312	0.078	0.039	0.000	20
7	1.25	1.25	0.312	0.312	0.156	0.078	0.039	24
8	1.25	0.625	0.312	0.312	0.078	0.078	0.078	24
9	2.50	2.50	0.625	0.078	0.039	0.039	0.000	20
10	0.156	0.625	0.312	0.312	0.156	0.156	0.078	24
11	0.312	2.50	2.50	0.312	0.039	0.039	0.039	24
12	0.625	2.50	0.312	0.156	0.078	0.078	0.039	24
13	0.312	0.625	0.312	0.078	0.039	0.000	0.000	16
14	0.625	1.25	1.25	0.156	0.039	0.039	0.078	24
15	0.625	1.25	0.625	0.078	0.000	0.000	0.000	12
16	0.078	0.156	0.078	0.625	0.312	0.078	0.078	24
17	0.312	2.50	1.25	0.078	0.078	0.000	0.000	16
18	0.078	0.078	1.25	0.039	0.039	0.039	0.156	24
19	0.312	0.625	0.625	0.312	0.039	0.039	0.039	24
20	0.156	0.625	0.156	0.156	0.156	0.156	0.312	24
21	0.078	0.078	0.156	0.078	0.000	0.000	0.000	12
22	0.156	0.625	0.312	0.078	0.078	0.078	0.039	24
23	0.625	0.625	0.312	0.156	0.078	0.039	0.039	24
24	2.50	1.25	0.156	0.312	0.156	0.039	0.000	20
25	0.312	1.25	0.156	0.078	0.156	0.078	0.039	24
26	0.312	0.625	1.25	0.156	0.078	0.000	0.000	16
27	0.156	0.625	0.156	0.078	0.078	0.039	0.000	20
28	1.25	1.25	1.25	0.312	0.039	0.000	0.000	16
29	0.156	0.078	0.078	0.078	0.078	0.078	0.039	24
30	0.312	1.25	0.625	0.156	0.078	0.039	0.000	20
31	0.312	1.25	0.625	0.039	0.039	0.078	0.039	24
32	0.312	0.625	0.625	0.078	0.039	0.000	0.000	16
33	0.625	1.25	0.625	0.078	0.000	0.039	0.000	20
34	0.625	1.25	0.625	0.078	0.039	0.078	0.039	24
35	0.312	0.625	0.312	0.156	0.078	0.039	0.078	24
36	0.312	0.625	0.625	0.312	0.039	0.039	0.078	24
37	0.625	0.625	2.50	0.078	0.156	0.078	0.039	24
38	0.156	0.156	0.156	0.156	0.039	0.078	0.078	24
39	0.078	0.156	0.039	0.156	0.039	0.078	0.156	24
40	0.312	1.25	0.625	0.312	0.039	0.039	0.078	24
41	0.312	0.312	0.625	0.625	0.312	0.156	0.078	24
42	0.625	1.25	0.625	0.156	0.078	0.039	0.039	24
43	0.625	0.625	0.625	0.312	0.156	0.039	0.039	24
44	0.156	1.25	0.312	0.312	0.039	0.039	0.156	24
45	0.312	0.625	0.625	0.312	0.156	0.156	0.156	24
46	1.25	1.25	0.312	0.312	0.078	0.039	0.039	24
47	0.625	0.625	0.312	0.312	0.078	0.156	0.078	24
48	2.50	1.25	0.156	0.312	0.156	0.039	0.000	20
49	0.625	1.25	0.625	0.078	0.000	0.000	0.000	12
50	0.625	1.25	0.625	0.078	0.039	0.078	0.039	24

units in 4.8 per cent beeswax by weight in peanut oil contained in 1 cc will produce and maintain assayable levels in the blood as follows: 0.33 cc (100,000 units) approximately eight hours, 0.5 cc (150,000 units) approximately twelve hours, and 0.66 cc (200,000 units) approximately sixteen hours. Evidence of a cumulative effect is furnished by

with three or four days after a single injection of 300,000 units.

A single injection of 2, 3 or 4 cc of the 300,000 units of calcium penicillin in 4.8 per cent beeswax by weight in peanut oil contained in 1 cc, totaling 600,000, 900,000 or 1,200,000 units, does not, as shown in Figure 3, double, triple or quadruple the

time for which assayable levels are present in the blood It does, however, produce extremely high levels Figure 3 also shows the amount and duration

TABLE 2 Penicillin Blood Levels Produced at 12 and 24 Hours after a Single Intramuscular Injection of 300,000 Units of Calcium Penicillin in 4.8 Per Cent Beeswax by Weight in Peanut Oil Contained in 1 cc

CASE No	TIME AFTER INJECTION		DURATION OF ASSAYABLE LEVEL (0.039 UNITS PER CC)
	12 HR	24 HR	
	units/cc	units/cc	hr
51	0 312	0 039	24
52	0 312	0 156	24
53	— *	0 625	24
54	0 625	0 000	12
55	0 625	0 078	24
56	0 078	0 156	24
57	0 156	0 039	24
58	—	0 000	?
59	—	0 000	?
60	—	0 156	24
61	—	0 078	24
62	—	0 078	24
63	—	0 156	24
64	—	0 039	24
65	—	0 039	24
66	—	0 039	24
67	—	0 039	24
68	0 625	0 039	24
69	—	0 078	24
70	—	0 312	24
71	—	0 000	?
72	0 312	0 078	24
73	—	0 000	12
74	—	0 156	24
75	—	0 078	24
76	—	0 000	?
77	—	0 039	24
78	—	0 156	24
79	0 312	0 156	24
80	—	0 000	12
81	0 156	0 039	24
82	0 625	0 000	12
83	—	0 312	24
84	—	0 078	24
85	—	0 039	24
86	0 312	0 039	24
87	0 078	0 000	12

*Blood not withdrawn for penicillin assay

of excretion of penicillin in the urine after the injection of these quantities

to suspend 495,000 units in 1 cc of beeswax and peanut oil This quantity would be equivalent in weight of penicillin to 300 mg One cubic centimeter of this mixture would theoretically produce adequate levels in the blood for somewhat over thirty-six hours

This and the data previously presented¹⁻³ suggest that the mechanism that causes the prolonged action of penicillin when suspended in beeswax and peanut oil is due to the following fact Beeswax and peanut

TABLE 3 Amount and Duration of Excretion of Penicillin in the Urine after a Single Injection of 300,000 Units of Calcium Penicillin in 4.8 Per Cent Beeswax by Weight in Peanut Oil Contained in 1 cc

CASE No	TIME AFTER INJECTION					TOTAL EXCRETION
	24 HR	48 HR	72 HR	96 HR	120 HR	
	units	units	units	units	units	units
47	151,135	6 500	940	0	0	158 575
50	136,105	29 300	1 031	198	0	166 635
81	154 000	7,370	1 360	27	0	162 757
82	179 000	975	244	85	0	180 304
87	116 000	10 300	1 340	195	0	127 835
Averages	147 248	10 889	983	101	0	159 221

oil when heated sufficiently yield a clear liquid, but when the mixture reaches approximately 37°C it becomes opaque, indicating that the beeswax is forming small particles In preparing the penicillin in beeswax and peanut oil³ it is the clear liquid that is added to the penicillin powder and blended until a complete suspension occurs When this final mixture cools to room temperature or 37°C, numerous minute particles of beeswax interspersed

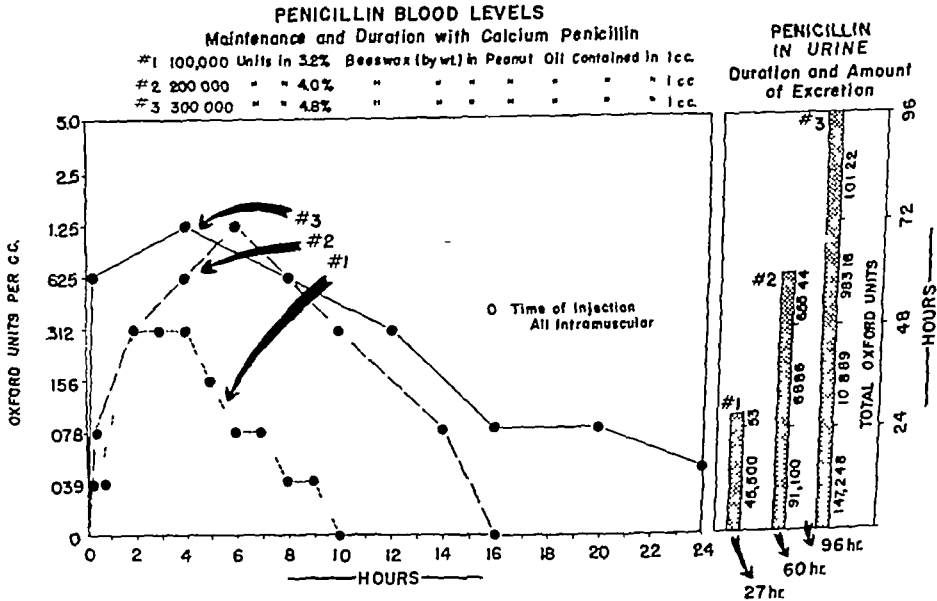


FIGURE 2

If crystalline penicillin assaying at 1650 units per milligram were available, it should be possible with minute granules of penicillin can be observed under the microscope This indicates that when

the penicillin in beeswax and peanut oil is injected intramuscularly at a temperature of 37°C, the particles of beeswax retard its absorption

should be adequate for all but overwhelming infections. It seems logical that the dose of penicillin should be the amount that will maintain ade-

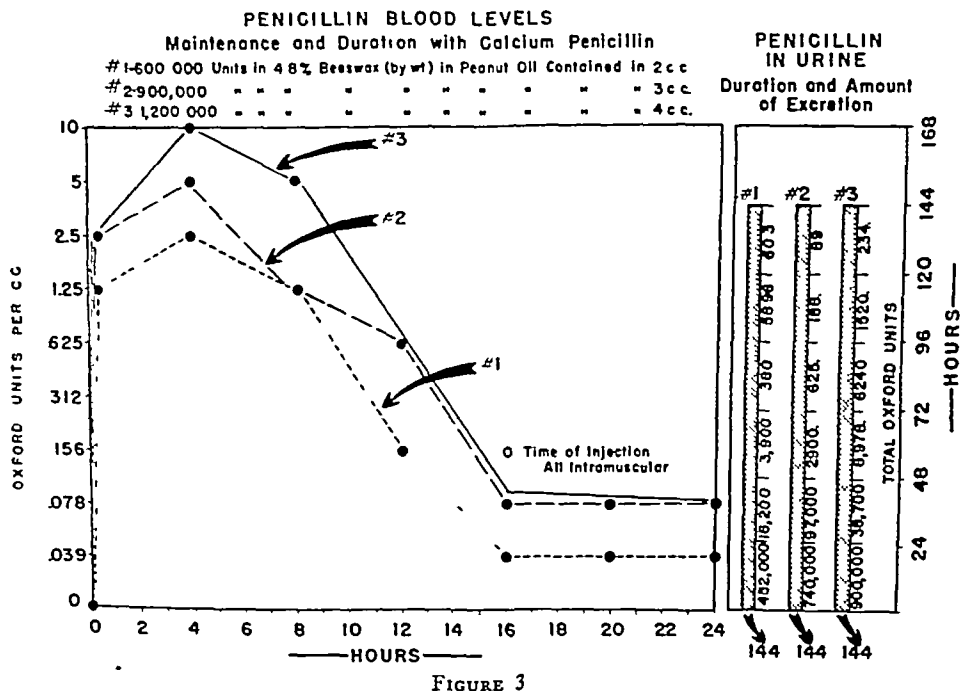


FIGURE 3

DISCUSSION

In view of the above and previous data, the following might be used as a basis of therapy A

quate levels of penicillin in the blood for twenty-four hours, rather than different quantities for each disease. Patients whose weight is 100 pounds or

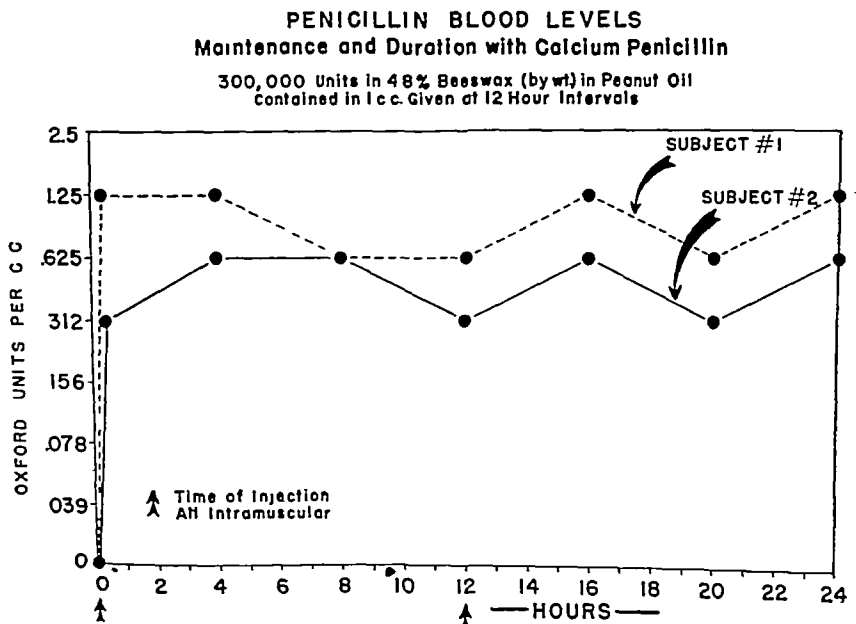


FIGURE 4

single daily dose of 300,000 units in 48 per cent beeswax by weight in peanut oil contained in 1 cc

less can be given 2000 units per pound and will maintain adequate penicillin levels in the blood

for twenty-four hours. For extremely severe infections, 300,000 units in 1 cc can be given at twelve-hour intervals, producing penicillin levels in the blood as shown in Figure 4.

Studies of the spinal fluid removed four hours after a single injection of 300,000 units of penicillin in 48 per cent beeswax by weight in peanut oil contained in 1 cc in 6 normal subjects gave no indication of the presence of penicillin at the lowest level assayable (0.039 Oxford units per cubic centimeter).

Duodenal drainage for removal of bile was done in 1 normal subject to determine the quantity of penicillin in the bile after a single injection of 300,000 units of calcium penicillin in beeswax and peanut oil. The bile was collected for a period of six hours after injection, and penicillin was found to be present at a level of 1 to 2 Oxford units per cubic centimeter.

Relative to the type of oil that has been used in the preparation of this mixture, it was found that sesame, corn or other oils might be used, but since the viscosity of these oils is less than that of peanut oil, it was always necessary to increase the amount of beeswax, which was not desirable. The peanut oil* in the mixture should have a moisture content of 0.05 per cent or less to maintain stability of the penicillin for nine or more months at icebox, room and 37°C temperatures. In addition, no deterioration of the calcium penicillin in beeswax and peanut oil occurs for twenty-four to thirty-six hours at 56°C or for two hours at 100°C. Details of the stability of the penicillin in this mixture will be reported soon.

The above data on stability indicate that the material should be kept at room temperature—except during long storage—and may be prepared for injection by one of the following three methods: three to five minutes under the hot-water tap (56 to 60°C), twenty to twenty-five minutes at 45°C, and thirty to thirty-five minutes at 37°C. The preparation is shaken at intervals so that there is thorough warming of all the material. After this, the mixture may be withdrawn with an 18-gauge or larger needle and injected with a 20-gauge needle. The penicillin in beeswax and peanut oil should not be forced into the 20-gauge needle until the needle has been inserted in the muscle, since the mixture

occasionally hardens in the metal needle, making it difficult to inject. A dry syringe and needle should *always* be used. Injections may be given in the upper outer quadrant of the buttock or in the deltoid, triceps or anterior thigh muscles.

As reported previously,³ calcium penicillin is essential, since the sodium salt is more hygroscopic and makes a granular suspension in the beeswax and peanut oil, which is occasionally difficult to inject, and since it produces levels that are erratic and not so prolonged as those obtained with the suspension of calcium penicillin. In addition, the sodium salt in beeswax and peanut oil does not consistently maintain its stability.

In addition to the 175 cases of gonorrhea already reported,² approximately 400 cases of gonococcal, pneumococcal, staphylococcal, streptococcal and other infections, including early syphilis and impetigo, have been treated by a single daily injection of penicillin in beeswax and peanut oil, with results comparable to those obtained by the daily multiple injections of penicillin in aqueous solution. These cases will be reported in the near future.

SUMMARY

A single injection of 300,000 Oxford units of calcium penicillin in 48 per cent beeswax (by weight) in peanut oil contained in 1 cc produces and maintains effective levels of penicillin in the blood for about twenty-four hours, and continues to be excreted in the urine for approximately three days.

Calcium penicillin in beeswax and peanut oil maintains its potency for at least nine months in a refrigerator, room and 37°C temperatures. In addition, there is no deterioration after twenty-four hours at 56°C or after two hours at 100°C.

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*This peanut oil was obtained through the courtesy of Dr. K. S. Markley, Southern Regional Research Laboratory, United States Department of Agriculture, New Orleans.

THE TREATMENT OF GONOCOCCAL URETHRITIS WITH SINGLE INJECTIONS OF PENICILLIN-BEESWAX-PEANUT OIL MIXTURES*

MAJOR WILLIAM LEIFER, M C, A U S, FIRST LIEUTENANT SAMUEL P MARTIN, M C, A U S,
AND FIRST LIEUTENANT WILLIAM M M KIRBY, M C, A U S

ROMANSKY and Rittman^{1, 2} have developed a practical and apparently safe procedure for retarding the absorption of penicillin by suspending it in a mixture of peanut oil and beeswax, and have reported favorable results in the treatment of gonococcal urethritis.

During the last nine months, various mixtures of penicillin in beeswax and peanut oil have been prepared and investigated at this hospital in an attempt to determine which one would produce the most satisfactory results, from the standpoint both of prolongation of blood levels and of clinical results. In the course of these studies, 217 men with acute gonococcal urethritis were treated with single intramuscular injections of one of these preparations. One hundred and forty-five patients were hospitalized for two days for the collection of blood and urine specimens, but were ambulatory. The remainder were treated as outpatients.

The patients had untreated, uncomplicated gonococcal urethritis, with the following exceptions: 4 had failed to respond to 100,000 units of penicillin in saline solution, given in four intramuscular injections of 25,000 units at three-hour intervals, 1 had failed after two such courses, 10 had failed after sulfonamide therapy, and 3 had epididymitis as well as urethritis.

All the patients had the characteristic clinical picture of acute gonococcal urethritis, with purulent urethral discharge, and the diagnosis was confirmed by smears and cultures. Following the single intramuscular injection of a penicillin-beeswax-peanut oil mixture, each patient was restricted to his military area for a period of twenty-one days, to obviate the possibility of reinfection. Post-treatment observations, consisting of a careful clinical examination, smear and culture of any urethral discharge and culture of the centrifuged urine sediment, were made on the second, seventh, fourteenth and twenty-first days.

The penicillin-beeswax-peanut oil mixtures were prepared in our own laboratory by mixing appropriate amounts of preheated, sterile, highly refined peanut oil† and bleached beeswax USP with powdered sodium or calcium penicillin in a mechanical blender until the penicillin was uniformly suspended throughout the oil and beeswax. The concentration of beeswax in the mixtures varied from 4 to 12 per cent by volume, and the penicillin content

from 100,000 to 300,000 units per cubic centimeter. The procedure and materials used were essentially the same as those described by Romansky and Rittman² and need not be repeated in detail. Similarly, the technic of injection requires no elaboration. It should be pointed out, however, that when 300,000 units of penicillin are suspended in 4 per cent beeswax, or when 100,000 units are suspended in 10 or 12 per cent beeswax, in a total volume of 10 cc, the mixtures are extremely viscous, even after being heated in an incubator or in a water bath at 37°C for thirty minutes. A 15-gauge needle was used to withdraw the mixtures into a syringe, and although considerable pressure on the plunger was required the material was injected into the buttock through a 20-gauge needle. The site of the injection was not massaged.

Assays of the blood and urine, which were performed in most of the cases, are briefly summarized later in this paper, and will be separately reported in detail.

No significant local or systemic manifestations of toxicity were noted following administration of the penicillin-beeswax-peanut oil mixtures. In most cases pain and tenderness were present at the site of injection for twenty-four to forty-eight hours, but these were no severer than when penicillin in saline solution is used.

Following the injection, clinical improvement was noted initially in all the 217 patients treated. Dysuria subsided during the first six to eight hours, and the purulent discharge became mucoid and watery. By the end of the second day almost every patient was free of symptoms and the urethral discharge had ceased. In general, the rapidity of clinical improvement was similar to that seen with penicillin in saline solution.

Of the 217 patients treated, 10 were followed for only seven days and 15 for only fourteen days, and none had clinical or bacteriologic evidence of relapse during that time, but since these patients did not fulfill the basic criterion of a twenty-one-day follow-up period, only the remaining 192, which were followed for twenty-one days, were considered in evaluating the results. Of these, 24 were failures (Table 1). In 10 patients there was a recurrence of urethral discharge, from which gonococci were cultured, in 8 of these relapse occurred by the seventh day, in 1 on the fourteenth day and in 1 on the twenty-first day. The other 14 failures were detected by bacteriologic methods alone — 7 on the seventh day, 3 on the fourteenth day, 1 each on the tenth and twelfth days and 2 on the twenty-first day.

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†The specially refined peanut oil was kindly supplied by the Southern Regional Research Laboratory, United States Department of Agriculture, New Orleans.

The relation of the total dose of penicillin to the percentage of cures is presented in Table 2. Of 88 patients treated with 100,000 units, 74 (84 per cent)

TABLE 1 *Cases of Failure Classified according to the Day after Treatment that Failure Was Detected*

CRITERIA FOR DIAGNOSIS OF FAILURE	No OF CASES	DAY AFTER TREATMENT THAT FAILURE WAS DETECTED							
		2	3	7	10	12	14	21	
Clinical and bacteriologic	10	3	2	3	0	0	1	1	
Bacteriologic only	14	0	0	7	1	1	3	2	
Totals	24	3	2	10	1	1	4	3	

were cured, and of 91 treated with 300,000 units, 83 (91 per cent) were cured. With 200,000 units, 11 of 13 patients were cured, but the numbers were too small to be significant.

In Table 3 the data are further subdivided to show the results in relation to the concentrations of bees-

TABLE 2 *Therapeutic Results in 192 Patients Observed for a Minimal Period of 21 Days and Classified according to Dose of Penicillin Administered*

DOSE OF PENICILLIN UNITS	No OF CASES	SUCCESS		FAILURE	
		NO	PERCENTAGE	NO	PERCENTAGE
100 000	88	74	84	14	16
200 000	13	11	85	2	15
300 000	91	83	91	8	9
Totals	192	168		24	

wax present in the various mixtures and to the salt of penicillin employed (sodium or calcium). In this group of cases sodium penicillin gave results equally satisfactory to those obtained with calcium penicillin, from the standpoint both of prolongation of blood levels and of therapeutic result. The total

TABLE 3 *Therapeutic Results Obtained with Various Penicillin Beeswax-Peanut Oil Mixtures in 217 Patients*

CONTENT OF BEESWAX*	SALT OF PENICILLIN	DOSE OF PENICILLIN UNITS	No OF CASES	SUCCESS		FAILURE
				FOLLOWED LESS THAN 21 DAYS	FOLLOWED 21 DAYS OR MORE	
4	Calcium	100 000	81	3	67	11
4	Calcium	200 000	8	0	7	1
4	Calcium	300 000	15	4	10	1
5	Sodium	300 000	9	1	8	0
5	Calcium	300 000	9	2	7	0
6	Sodium	100 000	5	2	1	2
6	Sodium	300 000	7	3	4	0
8	Sodium	100 000	4	0	4	0
8	Sodium	200 000	7	2	4	1
8	Sodium	300 000	34	3	29	2
8	Calcium	100 000	3	0	2	1
8	Calcium	300 000	13	3	9	1
10	Sodium	300 000	6	0	5	1
12	Sodium	300 000	10	2	8	0
12	Calcium	300 000	6	0	3	3
Totals			217	25	168	24

* By volume

number of units of penicillin in any given mixture was of much more importance in determining the results, from both the clinical and the laboratory standpoint, than was the salt of penicillin used.

All the 24 patients who were failures were eventually cured by further penicillin-beeswax-peanut oil therapy or by treatment with divided doses of penicillin in saline solution.

Of the 192 patients evaluated, 96 were Whites and 96 Negroes, with approximately equal racial distribution in the three penicillin-dosage groups. There were 10 failures (10 per cent) among the Negroes and 14 failures (15 per cent) among the Whites. This greater refractoriness of gonococcal urethritis in the latter, which has been noted many times with both the sulfonamide drugs and penicillin, is a factor to be considered in evaluating the results of therapy.

DISCUSSION

The observation of Romansky, Murphy, and Rittman³ that a single intramuscular injection of a penicillin-beeswax-peanut oil mixture is a highly effective method of treating acute gonococcal urethritis has been confirmed by the present studies. The results can be best evaluated by comparing them with those obtained with single or multiple injections of penicillin in saline solution. Of 100 men treated at this hospital with a single intramuscular injection of 100,000 units of penicillin in saline solution and followed both clinically and bacteriologically for a period of twenty-one days, 74 per cent were cured,⁴ as compared with the 84 per cent cured in the present series with a single injection of 100,000 units of penicillin in beeswax-peanut oil. The treatment of 600 men with 100,000 units of penicillin in saline solution in divided doses by several different time schedules resulted in 90 to 93 per cent cures,⁴ which compares favorably with the 91 per cent cures obtained in the present series with a single injection of 300,000 units of penicillin in beeswax-peanut oil. Thus, it appears that larger amounts of penicillin are required in single injections of the mixtures to produce results equivalent to those obtained with multiple injections of penicillin in saline solution.

Romansky, Murphy and Rittman reported 93 per cent cures of 100 patients treated with a single dose of 100,000 units and 100 per cent cures of 75 patients treated with a single dose of 150,000 units of a penicillin-beeswax-peanut oil mixture. Since the mixtures used by them were not identical with those of the present series, and since their cases were followed bacteriologically for only seven days, the results are not strictly comparable. Of the relapses in 24 cases in the present series, 9 occurred subsequent to the seventh day, and in these 7 patients failed to develop symptoms, the relapse having been detected by bacteriologic methods alone. The importance of a clinical and bacteriologic follow-up period of a minimum of twenty-one days, which is apparent from these observations, has also been emphasized by others. Recently, Lapenta, Weckstein and Sarnoff,⁵ using penicillin in saline solution, detected bacteriologic relapses up to nineteen days

following therapy, and concluded that, for proper evaluation of the results of treatment, cultures should be made at intervals for at least twenty-one days.

Under the auspices of the United States Public Health Service,⁶ 1060 patients, both male and female, with gonococcal urethritis or endocervicitis have recently been treated by single intramuscular injections of 200,000 units of penicillin in beeswax-peanut oil, with 91 per cent cures. These results are equivalent to those obtained with 300,000 units in the present series. The minimum standard for cure in the United States Public Health Service cases was a post-treatment observation period of at least ten days, with at least three negative cultures, including one on the tenth day of observation.

Assays of penicillin in the blood and urine were performed in most of the cases included in the present series and will be reported separately in detail. The information obtained from these assays clarified the clinical results. There was a striking variability of absorption and excretion with all the mixtures employed. With 100,000 units, assayable levels* were present in the blood stream for zero to sixteen hours, with the majority falling between four and eight hours. In a good many cases, levels could be detected for only four hours or less, a duration not significantly longer than that obtained with penicillin in saline solution, and sometimes not so long. Similar variability was observed when the mixtures contained 300,000 units of penicillin; assayable levels persisted for four to twenty-eight hours, and in most cases such a level was present for eight hours or more. This is roughly equivalent to the total duration of assayable levels obtained with 100,000 units of penicillin in saline solution when given in four intramuscular injections of 25,000 units each at three-hour intervals — that is, an assayable level for approximately two hours following each injection. There is apparently a relation between the duration of assayable penicillin in the blood and the clinical results. Thus, the results with 100,000 units of penicillin in saline solution, given in divided doses, were superior to those with 100,000 units of penicillin in beeswax-peanut oil, but were approximately equal to those with 300,000 units of penicillin-beeswax-peanut oil.

From the present studies, which included clinical and laboratory observations made with a variety of preparations, it appears that the penicillin-beeswax-peanut oil mixture used for the single-dose treatment of gonococcal urethritis should contain 200,000 or 300,000 units of penicillin, preferably the latter. Contrary to the impression of others, experience in this laboratory indicates that, from the standpoint both of prolongation of blood levels and of clinical results, sodium penicillin is as satisfactory as the calcium salt. Since concentrations of beeswax varying from 4 to 12 per cent produced closely

similar results, 4 to 6 per cent (by volume) in a total volume of 10 cc is recommended because such mixtures are less viscous and also contain less of the foreign material (beeswax). Preparations meeting these requirements — that is, 300,000 units of penicillin in 10 cc of a mixture of 4-8 per cent of beeswax by weight in peanut oil — are now being made for experimental study by several commercial houses, and one such preparation is under investigation in this laboratory at the present time. A report of the laboratory and clinical results with this material will be published elsewhere.

The two chief disadvantages of the beeswax-peanut oil mixtures are the larger amounts of penicillin required and the difficulty in heating and handling the viscous material. These disadvantages are, however, more than offset by the convenience of curing patients with a single intramuscular injection. Penicillin-beeswax-peanut oil mixtures offer the simplest and most practical method for the treatment of acute gonococcal urethritis in the office and the outpatient clinic. They may be useful in the treatment of diseases requiring prolonged and repeated injections of penicillin.

SUMMARY

Two hundred and seventeen men with gonococcal urethritis were treated with single intramuscular injections of 100,000 to 300,000 units of penicillin suspended in mixtures of beeswax and peanut oil. No local or systemic toxic manifestations were noted.

Of 88 patients treated with single injections of 100,000 units, 74 (84 per cent) were cured, and of 91 treated with 300,000 units, 83 (91 per cent) were cured. The results with 300,000 units of penicillin in beeswax-peanut oil were comparable with those obtained with 100,000 units of penicillin in saline solution given in divided doses, in other words, to produce equal results the mixtures required larger amounts of penicillin than did the saline solution.

All patients were followed for a minimum of twenty-one days, both clinically and bacteriologically. Of the failures in 24 cases, those in 9 occurred subsequent to the seventh day, and of these 7 were detected by bacteriologic methods alone. These results stress the necessity for a minimal post-treatment observation period of twenty-one days.

Assays of the blood and urine showed marked variability of absorption and excretion of penicillin following injections of the mixtures.

Sodium and calcium penicillin produced equally satisfactory mixtures, from both the clinical and the laboratory standpoint. Varying the concentration of beeswax from 4 to 12 per cent did not produce a significant difference in the results.

A single intramuscular injection of 10 cc of a mixture containing 300,000 units of penicillin in 4 to 6 per cent beeswax by volume in peanut oil appears to be a highly satisfactory method of treating acute gonococcal urethritis.

*The Kirby-Rantz modification of the Rammelkamp assay method was used, and the minimal assayable level by this method is 0.04 Oxford units of penicillin per cubic centimeter.

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SURGICAL RELIEF FOR TRACHEAL OBSTRUCTION FROM A VASCULAR RING*

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IN 1931, I performed an autopsy on a five-month-old baby who had had wheezing respirations since birth and had recently developed difficulty in swallowing. At this examination a ring of blood vessels was found encircling the intrathoracic portion of the esophagus and trachea in such a way that the esophagus was indented from behind, whereas the trachea was compressed on its anterior surface. The pathological findings at once suggested that a division of some part of the so-called "vascular ring" during life would probably have relieved the pressure on the constricted esophagus and trachea.

The above-mentioned case aroused my curiosity, and a rather extensive investigation of the literature has shown that quite a few examples of vascular ring have been found and described by various authors. Many of the observations have been made on aged adults receiving anatomical-room dissection, there having been no apparent symptoms during life. Conversely, some of the malformations have been uncovered in infants or children known to have had serious obstruction of the esophagus or trachea. The impression is gained that the majority of these vascular abnormalities give little or no symptomatology and are only incidentally discovered at post-mortem examination, but that in occasional cases the ring produces important complaints at an early age and indeed may lead to a fatal issue. Apparently, a vascular ring of large size is unlikely to give rise to symptoms, but in patients with a circle of relatively small size there are signs of esophageal and especially tracheal compression.

Vascular rings within the mediastinum are of two general types. In the first, the aortic arch is missing from its normal position in front of the trachea, and instead courses behind the esophagus. The pulmonary artery lies in a normal position in front of the trachea, but it is anchored to the distal part of the aortic arch by a patent ductus arteriosus—or a ligamentum arteriosum—at the left side of the esophagus and trachea. Hence, the esophagus is compressed from behind by the aortic arch and

the trachea is encroached on anteriorly by the pulmonary artery. It is conceivable that division of the patent ductus arteriosus or the ligamentum arteriosum would allow the pulmonary artery to fall forward and give sufficient room for the esophagus and trachea. The second general type of vascular ring is in effect a divided or split aortic arch. At a short distance above its valve, the aorta divides into two limbs. One of these passes posteriorly and then to the left behind the esophagus, and the other courses to the left in front of the trachea, the two merging in the left side of the mediastinum and forming the descending aorta. The innominate artery, the left common carotid artery and the left subclavian artery may all come from the anterior limb or from the posterior limb. More often, both limbs give rise to these various arteries. The limbs may be of approximately the same diameter, but one is apt to be larger than the other. A study of the previously recorded cases makes it obvious that the anatomic arrangements are frequently of a sort that make it impossible to divide any part of the ring without disturbing important vascular pathways. In other cases, however, it is certain that some part of the ring could be cut safely and that this would permit spreading of the ring to a degree that would relieve constriction of the esophagus and trachea.

In the following case, both types of vascular ring were present. First, the pulmonary artery was held tightly in a posteriorly displaced position by the ligamentum arteriosum, the division of which allowed the pulmonary artery to sag forward. Second, there was a split aortic arch, and division of its anterior limb immediately took considerable pressure off the anterior and left lateral surfaces of the trachea. So far as I know, this is the first patient for whom surgical division of a vascular ring has ever been attempted.

CASE REPORT

A 4-month-old infant was admitted on October 14, 1944, with a chief complaint of wheezing respirations since birth. Because of a widened superior mediastinal shadow, which was thought to represent an enlarged thymus, x-ray therapy was given. The patient was discharged on October 23, but was readmitted on November 13. There had been no improvement in the respiratory difficulty following the irradi-

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ation. For the last 24 hours there had been a cough, increasing distress during breathing efforts, fever, noisy respirations and a bout of vomiting.

Examination showed a seriously ill baby with extremely labored respirations. There was moderate intercostal retraction. Many coarse rhonchi were heard over both lung fields. The temperature was 101°F, and the white-cell count 12,800. The patient was thought to be suffering from an acute tracheobronchitis, and was placed in a steam room and given sulfadiazine. The fever gradually subsided to normal in 10 days. Five days later he appeared to be in fairly good condition and no longer showed intercostal retraction. However, noisy respirations and an intermittent cough continued throughout the hospital stay. He was discharged on December 2.

The patient was admitted for the third time on March 16, 1945. For 3 days there had been increasing wheezing, cough, dyspnea and fever. The cry had become hoarse. Coughing had greatly interfered with feeding and with sleeping. At times the breathing was quite labored.

Examination showed the patient to be in moderate respiratory distress. The temperature was 102°F, and the respirations 55. The mucous membranes of the throat were injected. There was moderate intercostal and suprasternal respiratory retraction. Throughout both lung fields were diffuse rales, which were particularly coarse during expiratory phases. The white-cell count was 18,700. A throat culture grew out moderate numbers of beta-hemolytic streptococcus and *Staphylococcus aureus*. Fluoroscopy showed an increased density in the region of the right middle lobe. Through the remainder of the chest there was a rather diffuse and patchy pneumonic infiltration.

The patient was immediately placed in a steam room, and sulfadiazine, as well as intramuscular penicillin, was started. During the first 24 hours his condition became distinctly worse. The temperature rose to 104.2°F, the respirations were much more labored, and cyanosis appeared. An oxygen tent gave some relief, but on the 3rd day the temperature again spiked to 104°F. Subsequently conditions improved, the temperature gradually subsided, the respirations became less labored, and the general appearance of the patient was less alarming. By the 7th day he had recovered sufficiently to be taken out of the steam room, and the penicillin was discontinued. Sulfadiazine was used until the 12th day. On the 11th day, a second roentgenologic examination of the chest showed widespread improvement of the lung, but the right middle lobe was still partially atelectatic. On April 3, bronchoscopy was performed and the orifice of the right middle lobe was found to be inflamed and possibly narrowed. On April 6, the patient was discharged in a fairly satisfactory state.

The fourth admission was on May 24, 1945. Since the previous discharge there had been persistent wheezing respirations, which, however, did not appear to interfere appreciably with the patient's health. For 4 days there had been increasingly severe cough and aggravation of the chest wheezing. The respirations had become extremely noisy, and saliva often accumulated in the throat and blocked the airway.

Examination revealed a well developed and well nourished infant in acute respiratory distress. He was breathing with great difficulty. There was moderate retraction of the suprasternal and intercostal spaces. The breath sounds were noisy and crowing. There were many coarse rhonchi throughout both lung fields. The temperature was 103°F, the white-cell count 12,250, and the red-cell count 3,480,000.

Immediately after admission to the ward the patient became quite cyanotic and was in collapse for a few hours. He was placed in an oxygen tent, and intramuscular penicillin was started. On the 2nd day, the respiratory signs were about the same, although the dyspnea had slightly decreased and the color was greatly improved. On the 3rd day the dyspnea had further diminished, the fever had disappeared, and the patient's general status was much better. By the end of a week he had almost completely recovered from the tracheobronchitis. There was still, however, a prominent wheezing sound during inspiration. This was especially noticeable during and after eating and was more audible when the respiratory efforts were increased by exercise and crying.

In an effort to detect some underlying abnormality that might have made the patient susceptible to repeated attacks of tracheitis, several investigations were undertaken. Roent-

genologic study revealed the following (Fig 1). Visualization of the esophagus in the anteroposterior view after a swallow of barium showed it to be very slightly narrowed opposite to the 3rd or 4th thoracic vertebra. At this level, the lateral view indicated a marked indentation of the posterior wall of the esophagus and a forward displacement of the esophagus. A mass appeared to lie between the esophagus and the vertebral column. Visualization of the trachea and

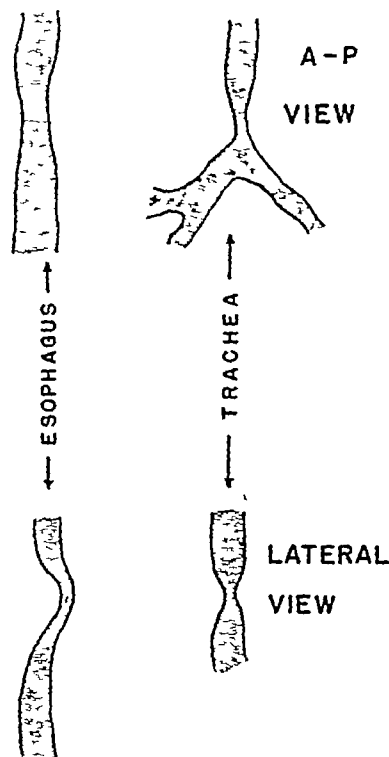


FIGURE 1 Tracings Made from Preoperative Roentgenograms (barium in the esophagus and lipiodol in the trachea)

In the anteroposterior view there is little narrowing of the esophagus but there is a definite narrowing of the trachea just above its bifurcation. In the lateral view the esophagus has a marked indentation on its posterior wall and the trachea has a distinct constriction.

bronchi after instillation of lipiodol showed a fairly marked narrowing of the trachea just above its bifurcation and at the general level corresponding with the previously described esophageal deformity. This narrowing was present in the anteroposterior view and was particularly prominent in the lateral film. There was no definite abnormality of the remaining portions of the tracheal or bronchial tree. Lipiodol freely entered the right middle lobe. These findings in the esophagus and trachea were interpreted by Dr. Edward Neuhauser as indicating the presence of a vascular ring.

Shortly after completion of the above studies, there was a sudden and severe flareup of the respiratory troubles. The respiratory rate rose, the pulse increased rapidly, and fever appeared. On the following day the respirations had reached 60, the pulse 160, and the temperature 103°F. At that time inspiratory and expiratory stridor was marked and there was intercostal and suprasternal retraction, as well as mild to moderate cyanosis. Sulfadiazine and penicillin were started.

Operation was performed on June 9. Although it might have been preferable to wait until all evidence of respiratory infection had disappeared, it was believed that the patient would have a better chance of combating the tracheitis if the trachea could be relieved of its mechanical obstruction. Operation was therefore proceeded with in spite of the precarious state of the patient. Under cyclopropane anesthesia

the chest was opened through a left anterolateral incision, with entrance to the pleural cavity through the third inter-space and division of the 3rd and 2nd costal cartilages. The left pleural cavity was traversed to reach the mediastinal structures. Opening of the mediastinal pleura and subsequent dissection of tissues gave an excellent view of the great vessels, all of which could be identified with certainty. A short distance above its origin, the ascending aorta divided into two limbs, which coursed upward to the left and joined to form the descending aorta (Fig 2). This divided arch formed a ring that enclosed and greatly constricted the esophagus and trachea. The innominate artery, the left common

portion of the arterial ring that encircled the esophagus and trachea. If the posterior branch of the split aortic arch had been smaller than the anterior one, I should have preferred to cut it, since this would have more nearly returned the vascular system to a normal arrangement. However, since the posterior branch was the larger of the two limbs, it was believed that division of the anterior one would give less interference to the supply of blood to the descending aorta. The anterior aortic arch was severed as indicated in Figure 3. When this was done, the left common carotid artery immediately displaced superiorly and toward the right and the trachea was obviously relieved of most of the existing

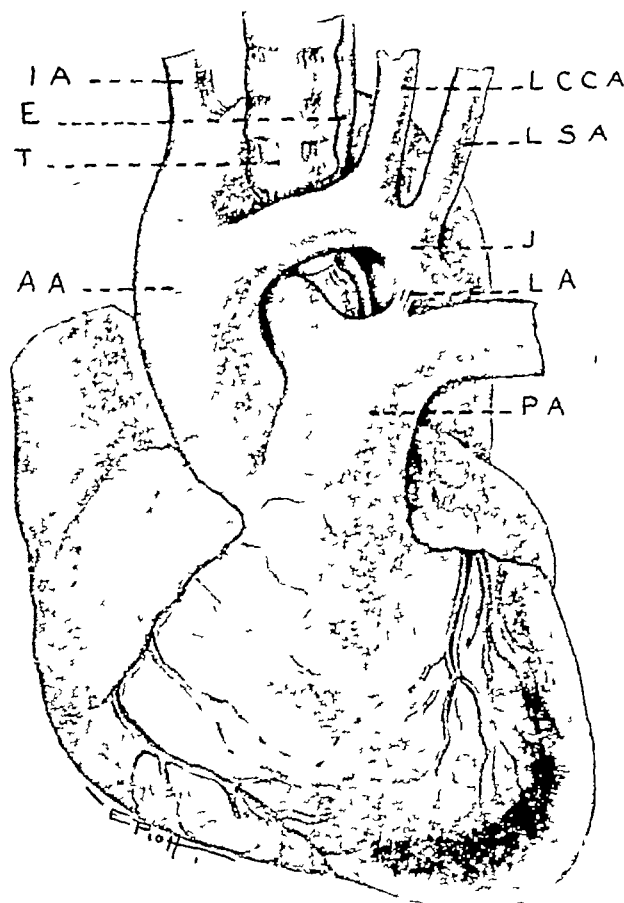


FIGURE 2 Arrangements of the Great Vessels as Found at Operation

The ascending aorta bifurcates into two branches, one passes behind the esophagus, and the other arches in front of the trachea. The two branches join to form the descending aorta. Within the vascular ring the esophagus and trachea are compressed. AA — ascending aorta, E — esophagus, IA — innominate artery, J — junction of the two aortic arches, LA — ligamentum arteriosum, LCCA — left common carotid artery, LSA — left subclavian artery, PA — pulmonary artery, and T — trachea.

carotid artery and the left subclavian artery arose as indicated in the illustration. The pulmonary artery seemed to be held tightly against the anterior surface of the trachea by its attachment — through the ligamentum arteriosum — to the aorta.

After all the above anatomic findings and variations had been carefully identified, steps were taken to relieve the tracheal compression. First, the ligamentum arteriosum was divided between silk ligatures to allow the pulmonary artery to fall forward and away from the trachea. This had some slight beneficial effect on the respiratory exchange, but it was not marked. It was then decided to divide some

compression. During the first part of the operation the respiratory distress caused extreme anxiety, there was a loud and prominent inspiratory and expiratory crow, and the pronounced shift in the mediastinum with each of the respiratory movements made the dissection quite difficult. As soon as the anterior aortic arch had been divided, however, the respirations quieted down, most of the crowing disappeared, and the respiratory shift in the mediastinum diminished to a normal degree. The chest wall was closed in an appropriate manner, the left lung being completely expanded before final repair of the wound.

To combat the residual tracheal infection, the patient was

placed in a steam room for 1 week and was given parenteral sulfadiazine and penicillin for 16 days. By the 5th post-operative day, the fever had gradually disappeared, the pulse had slowed to a normal rate, and the respirations had fallen to 25 or 30. The wound healed per primam. After 1 week, the acute stage of the tracheal infection had disappeared and the respiratory system appeared to become stabilized. The effects of the operation could then be evaluated. The patient was alert and playful and had no distress of any kind. With the ear held close to the chest a faint inspiratory sound could be heard. During and immediately following deglutition of food these inspiratory sounds became

the long-standing external pressure that had existed throughout the life of the patient. During the final week of observation on the ward, the patient's general condition was entirely satisfactory. The respirations were barely audible, but the patient appeared contented and playful and was completely free of any respiratory embarrassment.

SUMMARY AND CONCLUSIONS

The case is reported of an infant who was proved to have tracheal compression from a vascular ring.

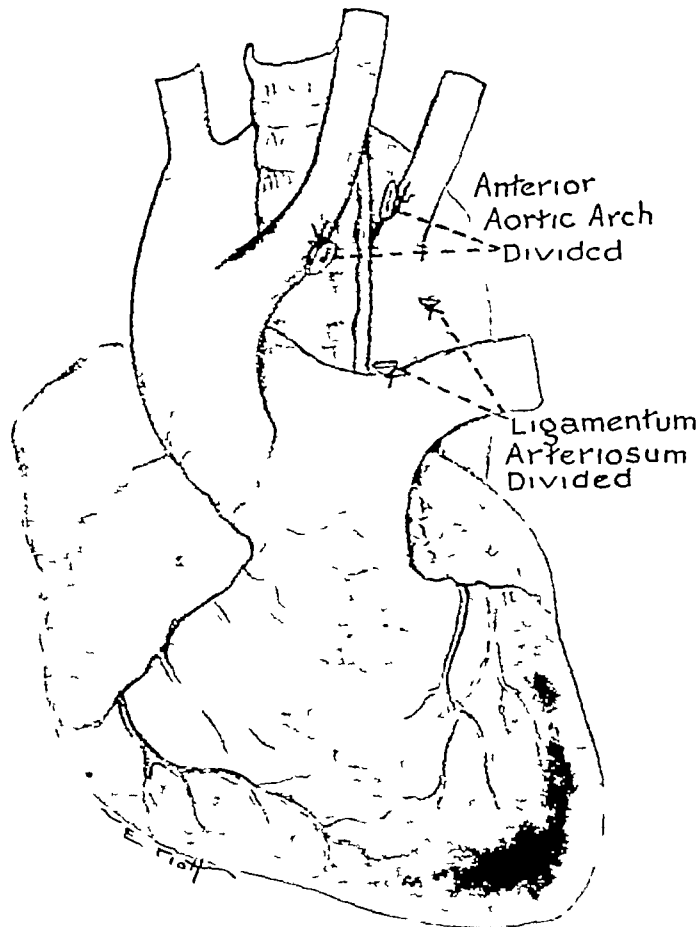


FIGURE 3 Surgical Procedure
The ligamentum arteriosum was divided to allow the pulmonary artery to displace forward. The anterior arch of the aorta was divided to relieve compression of the trachea.

slightly louder — apparently because the esophagus was still displaced forward by the aortic arch behind it and was causing some pressure on the posterior wall of the trachea. On July 7, roentgenographic examinations were again performed to visualize the esophagus and trachea. There was no change in the esophagus from its preoperative state. The trachea still presented some narrowing above its bifurcation, but this was distinctly less marked than it had been before operation. Although there was some indentation along the right side of the trachea, the left border had straightened out considerably following the operative procedure. The deformity that remains in the trachea may be due to some residual pressure from the left common carotid artery or to incomplete development of the tracheal ring following

within the mediastinum. The tracheal obstruction was particularly troublesome because of repeated attacks of superimposed tracheitis, for which the patient was hospitalized on four different occasions. Roentgenologic studies showed evidence of a vascular ring, and at operation the vessels were suitably divided to allow sufficient room for the trachea. The patient tolerated this surgical procedure extremely well and has had marked alleviation of symptoms.

The detection of a vascular ring is apparently not difficult. Since in the vast majority of these patients some portion of the vascular ring passes behind the esophagus, fluoroscopic observation after a swallow of barium should show indentation of the posterior wall of the esophagus. If such esophageal deformity is found, the trachea can be studied by the introduction of lipiodol and by ap-

propriate film studies in the anteroposterior and the lateral views, to detect any constriction of the trachea that may exist. Vascular rings do not always give rise to important clinical symptoms, but when the compression of the trachea is great enough to give rise to respiratory distress, surgical division of some portion of the ring should offer an excellent chance for relief of symptoms.

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DEATH FOLLOWING THE INTRAVENOUS ADMINISTRATION OF PAPAVERINE HYDROCHLORIDE*

A Report of Two Cases

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THE intravenous administration of papaverine hydrochloride has been recommended in the treatment of peripheral embolism, pulmonary embolism, mesenteric embolism, impending gangrene due to ergot, Raynaud's disease, angina pectoris, acute myocardial infarction, cardiac arrhythmias, renal and biliary colic and bronchial asthma and for the measurement of the circulation time.¹⁻¹² Most discussions of its clinical employment stress its low toxicity and contain a paucity of warnings concerning possible dangers. Pal,¹ who originally advocated its use, implied that the intravenous administration might be dangerous and used only small doses by that route. Elek and Katz¹¹ concluded that intravenous injection may be contraindicated in complete auriculoventricular dissociation because they observed a short period of ventricular tachycardia following intravenous administration of the drug in a patient with complete heart block. Gray, Riseman and Stearns¹² observed severe reactions following the intravenous injection of papaverine hydrochloride in patients with coronary artery disease, and point out that the intravenous administration of drugs to such patients is not without danger.

We have recently encountered 2 deaths following the intravenous use of papaverine hydrochloride. Since a careful search of the literature has revealed no fatalities from this cause, these cases are being reported.

CASE 1 H. F., an 80-year-old man, collapsed because of weakness of the legs on the morning of admission to the hospital. The past history was negative except for prostatectomy 5 years previously, occasional edema of the ankles and slight dyspnea on exertion.

Physical examination revealed slight mental confusion, emphysematous but clear lungs and an enlarged heart with

faint sounds, irregular rhythm and a loud apical systolic murmur. The blood pressure was 160/70. The peripheral vessels were sclerotic, and dorsalis pedis pulsations were absent. Two urine examinations were negative. Blood-cell counts, a blood smear and the nonprotein nitrogen level were normal. Blood Hinton and Kahn reactions were negative. An electrocardiogram showed auricular fibrillation, multiple ventricular ectopic beats arising from different foci, left-axis deviation, a diphasic T₁, an inverted T₂ and a normal Lead 4F.

Diagnoses of generalized arteriosclerosis, arteriosclerotic heart disease, auricular fibrillation, pulmonary emphysema and possible cerebral embolism were made. The only medications given were tincture of digitalis and chloral hydrate.

On the 4th day, the patient complained of pain in the legs. Examination revealed no change in physical or mental status except for the limbs, which showed paralysis, decreased temperature, absent pulsations and areas of blotchy livid discoloration extending up to 3 cm below the umbilicus. A diagnosis of embolus to the bifurcation of the aorta was made.

Two cubic centimeters (0.065 gm) of papaverine hydrochloride was given intravenously. Thirty to 40 seconds after completion of the injection the face suddenly became flushed and there was deep and rapid respiration for 1 minute. During this period the eyes rolled up and to the left, the head fell back, and the heart sounds were inaudible. The period of tachypnea was followed by apnea interrupted by several deep gasping breaths. The patient was pronounced dead 5 minutes after the injection of papaverine hydrochloride. Permission for post-mortem examination was not obtained.

CASE 2 (private patient of Dr. Nathan T. Bresnick) E. G., a 61-year-old woman, was admitted because of epigastric pain, fever and chills occurring 3 weeks after low amputation of the left thigh. Similar symptoms lasting for 24 hours had occurred the day following the amputation. The past history was negative except for diabetes mellitus for 11 years.

Physical examination revealed a rectal temperature of 103°F, a blood pressure of 138/92, an enlarged heart with a soft systolic murmur heard all over the precordium, dullness and fine crackling rales at both lung bases and pitting edema of the right leg. Urine examination was negative except for slight albuminuria and a few white cells in the sediment. The red-cell count was 3,350,000, the hemoglobin 68 per cent (Sahli), the white-cell count 16,650, and the fasting blood-sugar 205 mg per 100 cc. An electrocardiogram showed normal rhythm, left-axis deviation, a small Q₁, a prominent Q₂, diphasic T₁ and T₂ and inverted T₃ and T₄ (Lead 4F).

The diagnosis of pulmonary embolism with infarct of the right lower lobe of the lung was made. Penicillin therapy was instituted, and on the 2nd day bilateral ligations of the femoral vein were performed. During the next few days the temperature fell to normal. Starting on the 5th day, however, the patient had episodes of sweating, weakness, dyspnea and apprehension and a pressing sensation in the anterior

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region of the chest. Examination during these periods showed dyspnea and rales throughout both lungs. It was thought that these episodes represented paroxysmal pulmonary edema occurring with or precipitated by angina pectoris or pulmonary emboli.

On the 10th day, during one of these episodes, the patient was given oxygen and a subcutaneous injection of 0.015 gm of morphine sulfate and 0.0005 gm of atropine sulfate. There was only slight relief of symptoms in 15 minutes, and an intravenous injection of 1 cc. (0.03 gm) of papaverine hydrochloride was given. Thirty seconds later the patient took several deep breaths in rapid succession, followed by a period of apnea. The heart sounds were inaudible. During the next 2 or 3 minutes artificial respiration was carried out and 2 cc of Coramine and 1 cc of epinephrine hydrochloride (1:1000) were given intravenously. Except for a few gasping breaths, however, neither respiration nor heart action could be restored, and the patient was pronounced dead 5 minutes after the intravenous injection of papaverine hydrochloride.

Autopsy. There was 200 cc. of serous fluid in both pleural cavities, the major branch of the pulmonary artery leading to the right lower lobe of the lung contained an adherent thrombus, and there was a recent infarct in this lobe. The heart showed no evidence of myocardial infarction, but there was an old occlusion of the right coronary artery and several points of narrowing in both major coronary arteries. Otherwise the examination was essentially negative.

DISCUSSION

Previous reports have shown that untoward reactions may occur after the intravenous injection of papaverine hydrochloride. In animals, excitement, cardiac arrhythmias, respiratory distress and death, occurring with convulsions, ventricular fibrillation or respiratory arrest, have been described following administration of large doses.¹³⁻¹⁹ In man, cardiac arrhythmias, respiratory disturbances and vasomotor reactions have been observed after the intravenous injection of therapeutic doses (0.03 to 0.13 gm).^{6, 10-12} The respiratory changes have been frequently noted and are described by Elek and Solarz¹⁰ as the end point for the measurement of the circulation time. In most cases the symptoms experienced are not severe and are well tolerated. Gray, Riseman and Stearns,¹² however, mention several patients in whom severe reactions were encountered.

In the 2 cases reported herein death occurred following hyperpnea and tachypnea, which became manifest approximately thirty seconds after completion of the injection. Initially these abnormal respirations were similar to those frequently observed following intravenous administration of the drug. In the present cases, however, they marked the cessation of normal respiratory rhythm, being followed by apnea and a series of terminal gasping breaths. The heart sounds were not audible after the onset of respiratory symptoms, and death may have occurred as the result of either a cardiac or a respiratory disturbance. The mode of death was apparently an extension of the reactions generally encountered after the intravenous administration of papaverine hydrochloride.

In the cases described, death occurred within five minutes of the intravenous injection of papaverine hydrochloride, the duration of injection ranging from thirty seconds to one minute. Both patients were acutely ill at the time of injection but not moribund, and there was an abrupt unexpected change in their condition approximately half a minute after the injection. The chronological sequence and the symptoms observed suggest that the sudden death was related to the administration of the drug.

SUMMARY AND CONCLUSIONS

The intravenous administration of papaverine hydrochloride has been advocated in the treatment of a variety of conditions, in some of which its value is questionable. Although reactions have been observed following its intravenous use in man, most authors believe that there is little if any contraindication to its use by that route. The 2 cases reported herein show that the toxicity of papaverine hydrochloride is not so low as has previously been believed, for intravenous administration is apparently capable of causing death.

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RHEUMATOID ARTHRITIS· ITS VARIED CLINICAL MANIFESTATIONS*

MARIAN W ROPES, M D,† AND WALTER BAUER, M D ‡

BOSTON

ONE of the greatest difficulties in recognizing rheumatoid arthritis, except in a severe, advanced form, arises from the fact that the disease may have many types of onset and may vary greatly in its course.¹⁻⁶ It often resembles other types of joint disease so closely that incorrect diagnoses are made and proper therapy is not instituted at a time when it is most beneficial.

The typical picture of rheumatoid arthritis is well known in its fully developed form.¹⁻⁹ Unfortunately, it is the severe, crippling stage that most physicians and patients visualize when the word "arthritis" is mentioned. Even in these typical cases, however, the early stages are not well recognized. Often prodromal symptoms of fatigability, anorexia, weight loss, and numbness and tingling in the extremities, with or without vague muscle and joint aching, precede joint manifestations by many months or years. Precipitating factors, such as physical or emotional strain, infections and accidental or operative trauma, often appear to play a role both in the initiation of the prodromal symptoms and in the production of articular manifestations of the disease. Characteristically in severe cases, the constitutional symptoms steadily increase and there is progressive, symmetrical involvement of many joints. The articular changes consist of pain, tenderness, swelling, — often with effusion, — thickening of periarticular tissues and limitation of motion with increasing deformities. Vasomotor symptoms, chiefly manifested by cold, moist hands and feet, are prominent in at least two thirds of the cases. Numbness and paresthesias in the extremities are of common occurrence. In severe cases, extreme atrophy of skin, muscles and bones occurs. The involvement of many nonarticular systems is made evident by the finding of anemia, lymphadenopathy, splenomegaly, subcutaneous nodules, iritis, pleurisy, pericarditis and myocarditis. The course in typical cases, even if untreated, is characterized by more or less complete remissions after varying periods of activity, often followed by subsequent exacerbations. In severe cases, the joints may show increasing residual damage after each exacer-

bation. Treatment, which will be discussed later, appears to hasten remissions and possibly prevent exacerbations.

The many variations in the onset and course of rheumatoid arthritis can best be made apparent by the presentation of cases. A typical case of moderate severity will be described first, and this can be used as a basis of comparison for the other forms of the disease as manifested in the subsequent case reports.

CASE 1 A 49-year-old, unmarried waitress was admitted to the hospital on October 15, 1932, complaining of joint pains of 6 months' duration. Early in 1932 she noticed easy fatigability and frequently experienced numbness of the hands. In April, 1932, the right shoulder suddenly became stiff and painful. These symptoms subsided in 3 days, but 2 weeks later the left ankle became swollen, tender and painful. Subsequently the right knee, the 2nd and 3rd left metacarpophalangeal joints, the right wrist and the jaws were similarly affected. The patient noted nervousness and weakness and lost 15 pounds in weight. The hands and feet were frequently cold, numb and moist.

The past history was of importance because the patient had had many operations and infections. She had had pleurisy on several occasions, typhoid fever in 1896, appendectomy in 1913, tonsillectomy in 1914, bilateral radical antrum operations in 1920, cholecystectomy, hysterectomy and bilateral oophorectomy in 1923 and a right-sided mastoidectomy in 1927. She had always had frequent colds, and for many years there had been some discharge from the right ear.

Examination on admission revealed a poorly developed, undernourished woman. There was slight arteriosclerosis of the vessels of the fundi and tenderness over both antrums. A few coarse râles were heard at the base of the left lung. The liver and spleen were palpable. Joint examination showed limitation of jaw motion, slight stiffness of the neck and swelling and tenderness of all the metacarpophalangeal and midphalangeal joints, the left knee, the left ankle and the left metatarsophalangeal joints. The laboratory findings were normal except for a corrected erythrocyte sedimentation rate of 135 mm per minute. X-ray examination showed atrophy of the bones around the involved joints and narrowing of some of the phalangeal joints. Tonsillar tabs were removed on October 28, 1932. The symptoms and joint changes increased during the first 4 weeks after admission but slowly subsided during the last 6 weeks in the hospital. Treatment consisted of bed rest, exercises, hot packs on involved joints, antral washes, aspirin and added vitamins.

Following discharge, the patient continued to improve and by May, 1933, was free of all symptoms except slight and by May, 1933, was free of all symptoms except slight fatigability and slight pain in the left knee. On examination, however, there remained slight periarticular thickening of the midphalangeal joints of both hands and slight swelling of the left knee. She remained relatively well until October, 1933, about 1 month after she had returned to work, when there was recurrence of fatigability and of pain and swelling in both hands, wrists, knees, left ankle and left foot. These symptoms again slowly subsided, and the patient became symptom free in June, 1934. At that time the joints were normal except for slight swelling of the 2nd and 3rd midphalangeal joints of the right hand and slight tenderness of the metatarsophalangeal joints of both feet. The sedimentation rate, however, remained elevated.

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The patient felt well until December, 1934, when symptoms began to recur following a period of severe emotional strain occasioned by incompatibility with the people with whom she was living. This exacerbation was of somewhat shorter duration than the previous one, the symptoms and most of the signs having disappeared by May, 1935. Since that time she has continued to have exacerbations of varying severity and duration. The usual precipitating factors have been emotional strain and, less frequently, overactivity or respiratory infections. She has had frequent attacks of bronchitis, and chest x-ray films have shown evidence of bilateral bronchiectasis. During remissions she has been relatively free of symptoms and has been able to carry on moderate activity. There has been some tendency for increasing deformities of joints following the repeated exacerbations of the disease. The only abnormalities found on examination of the joints in June, 1945, however, were slight swelling of the metacarpophalangeal and midphalangeal joints of both hands, slight limitation of motion of the neck, both shoulders, the left wrist and the right knee, limitation of extension and flexion of the right wrist to 20°, and a flexion deformity of 20° in the left knee.

fixed, changing very little during exacerbations and remissions.

In many cases of rheumatoid arthritis the onset and course vary greatly from those of the typical case described above and often duplicate those of other forms of joint disease. In the following case the sudden febrile onset after an acute infection, the skin rash and the migratory joint involvement with localization in a few joints led to a diagnosis of infectious arthritis. The subsequent course and findings made it apparent that the patient had rheumatoid arthritis.

CASE 2 A 38-year-old, unmarried music teacher was first admitted to the hospital on February 3, 1934, because of fever and painful joints of 4 weeks' duration. The family history revealed that her maternal grandmother had had generalized arthritis for many years. The past history was

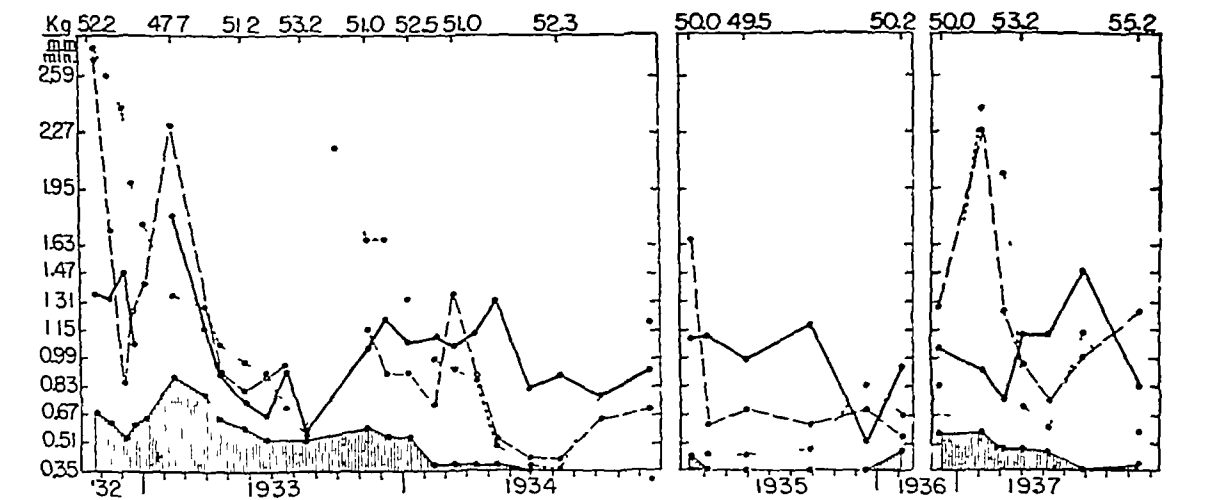


FIGURE 1 Graphic Presentation of the Course of the Disease in Case 1 during the Period from 1932 to 1937. The solid line represents the sedimentation rate, the dotted line the subjective symptoms, and the broken line the objective joint findings. The shaded area represents that portion of the objective findings that is due to limitation of joint motion. In obtaining the subjective and objective figures, an arbitrary scale was employed assigning a value to each symptom and sign in each joint. The subjective symptoms include joint pain and stiffness, fatigue, malaise and general disability. The objective findings include the pain, swelling, tenderness and limitation of motion of the joints. The body weights are recorded at the top of the figure.

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The course of the disease between 1932 and 1937 is presented graphically in Figure 1. It is of significance that the sedimentation rate never returned to normal during remissions. A comparison of the sedimentation rate with the subjective and objective findings indicates that the rate reflected the clinical changes well during the early stages of the disease but subsequently became relatively

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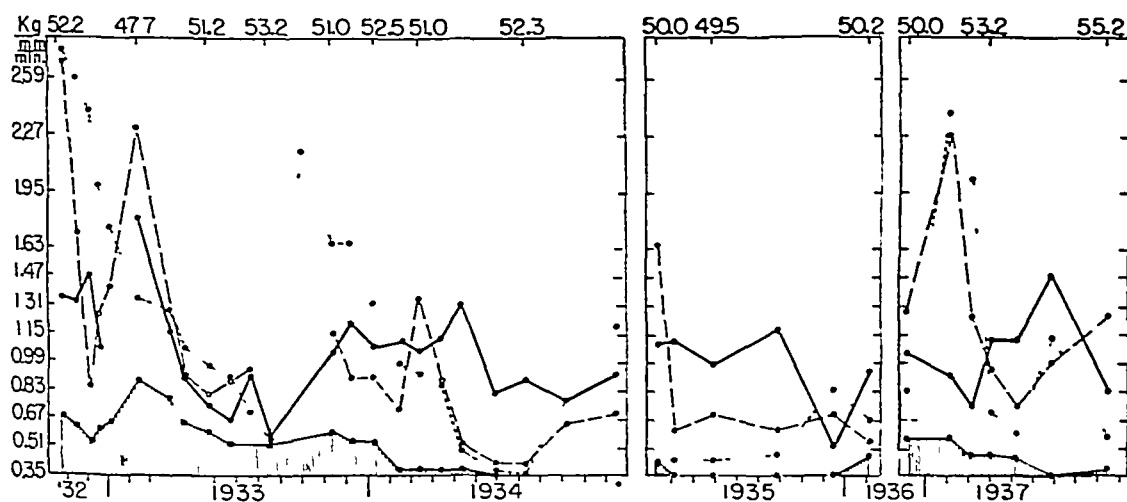


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Specimens of the urine showed an occasional trace of albumin and on several occasions contained many leukocytes. The white-cell count was 22,000 on admission and subse-

quently fell to 9000. The red-cell count rose from 3,400,000 to 4,300,000, and the hemoglobin from 50 to 85 per cent (Sahl). The corrected sedimentation rate varied from 1.00 to 1.50 mm per minute. Blood and urine cultures were negative. Synovial fluid aspirated from the left knee showed a white-cell count of 9500, with 90 per cent polymorphonuclear leukocytes.

For 8 weeks the patient ran a spiking temperature with swings from 98.6 to 104 or 105°F, except for periods of 2 or 3 days during which the temperature remained around 100°F.

Tonsillectomy and adenoidectomy were performed 9 weeks after admission, at the end of this febrile period, without obvious effect on the course of the disease. Blood transfusions were given on two occasions. The right pleural cavity was tapped on April 25 and a few cubic centimeters of clear, yellow fluid containing 810 mononuclear cells per cubic millimeter was obtained. During the first 3 months of illness the patient lost 30 pounds, but regained 20 pounds before discharge. At the time of discharge in June, 1934, slight fatigability persisted, but all joint symptoms except migratory aches had subsided. Examination of the chest showed the same signs as at entry. The joints were normal.

During the 6 months following discharge all symptoms disappeared, and the sedimentation rate fell to 0.5 mm per minute. The patient remained well until March, 1936, when she had a severe sore throat and developed pain in almost all joints, including the temporomandibular and sternoclavicular. These symptoms subsided in 2 months. Since that time she has continued to have occasional aches in various joints, with exacerbations of joint pain and swelling during respiratory infections or after periods of physical or emotional strain. Such exacerbations have persisted for many weeks. The sedimentation rate has risen to approximately 10 mm per minute during these attacks but has fallen almost to normal during remissions. X-ray films taken in 1943 showed slight narrowing of the midphalangeal joints of the hands and feet and slight atrophy of the bones around the wrists and the metatarsophalangeal joints. During the exacerbations there has been marked fatigability. The involved joints are painful on motion and are often swollen.

Many of the features presented by this case are not generally recognized as characteristic of rheumatoid arthritis. The onset of the major attacks during respiratory infections is not unusual. In our experience the first joint manifestations of rheumatoid arthritis have been precipitated by infection in at least 20 per cent of the cases. Daily elevation of the temperature to 105°F, comparable to that seen in this case, may persist for more than a year in rheumatoid arthritis. Skin lesions resembling rashes of many types often appear during the active stage. The occurrence of pleurisy with effusion is less frequent but is occasionally observed. The similarity of the attacks that occurred at the ages of nine and thirty-eight is striking. It is probable that involvement of the temporomandibular joints in the first attack led to the recession of the jaw that was apparent at the time of admission to the hospital twenty-nine years later. In fact, the story of the childhood illness was obtained only on direct questioning after the observation of the jaw recession had suggested the probability that such an attack had occurred. The long remission between the attacks is not unusual.

The resemblance of rheumatoid arthritis to infectious arthritis is frequently seen in less severe cases than the above. In the following case, the sudden onset of joint symptoms and the exquisite pain and tenderness in the severely involved joints suggested the possibility of infectious arthritis,

presumably gonococcal. The laboratory studies and the subsequent course failed to corroborate such a diagnosis and demonstrated that the patient had rheumatoid arthritis.

CASE 3 A 28-year-old machinist was admitted to the hospital on October 24, 1935, because of pain and swelling of the knees of 5 weeks' duration. The past history was not significant except for an attack of pain and stiffness in the left knee in 1931. Six weeks before admission the patient had an upper respiratory infection, and 1 week later developed pain in the temporomandibular joints. Three days later the pain in the jaws disappeared but the right knee became swollen and painful. Four weeks later the left knee and left shoulder became involved.

At the time of admission the temperature was 102°F. The general examination was negative. Both knees contained effusions and were tender. The right knee and hip could not be moved because of severe pain. A few days later the left wrist became swollen, hot and tender. The blood cell counts were normal and urine examinations were negative. The corrected sedimentation rate was 1.88 mm per minute. A gonococcal complement-fixation test gave a negative reaction, and prostatic smears showed no gonococci. Synovial fluid aspirated from the left knee contained 6300 white cells per cubic millimeter, 63 per cent of which were polymorphonuclear leukocytes. X-ray examination of the left knee was negative.

The symptoms subsided steadily, and at the time of discharge on November 23, 1935, joint examination showed only slight thickening of the tissues around the knees. Some stiffness of the knees, left wrist and neck continued for approximately 4 months after discharge, and during this period the patient frequently noted slight swelling of the right ankle. Thereafter he remained free of symptoms except for occasional pain in the knees or the lumbar region of the back until September, 1938, when the pain in the back began to recur each morning. In October, 1938, while sawing wood for many hours a day, he noted easy fatigability, developed slight stiffness in his knees and feet and lost 10 pounds in weight. The chest expansion at this time was only 4 cm. In December all the symptoms except slight pain in the back had subsided, although the patient continued to lose weight.

He then remained essentially symptom free for 6 years. During this interval he regained weight and the chest expansion increased to 9 cm. In 1943 his hours of work increased to 60 or 70 a week. There was no associated change in symptoms, but the sedimentation rate became elevated in October, 1943, for the first time in 6 years and the patient began to lose weight. One year later, following an upper respiratory infection in September, 1944, he had an exacerbation of his disease, with loss of weight and fatigability, as well as pain, stiffness and slight swelling in the metacarpophalangeal and midphalangeal joints of both hands and pain in the lumbar region of the back. With increased rest in bed and a reduction in the hours of work, the majority of the symptoms subsided within a month, although slight fatigability has continued.

The course of the arthritis in this case is presented in graphic form in Figure 2. It offers an interesting contrast to that of Case 1 (Fig 1). In general, the sedimentation rate reflected the clinical course. It is noteworthy, however, that the rate did not return to normal for many months after the subjective and other objective evidences of disease had disappeared. Furthermore, the rise of the sedimentation rate in the last exacerbation preceded the clinical manifestations by many months. A fall of the rate to normal during remissions in general suggests a good prognosis, as in this patient, whose disease has remained in remission except on two occasions when exacerbations were precipitated by overwork.

Not infrequently, as exemplified by Case 4, the onset of rheumatoid arthritis resembles that of rheumatic fever and final diagnosis often cannot be made until the patient has been followed for many months.

CASE 4 An 8-year-old girl was admitted to the hospital on February 24, 1942, because of joint pains and swelling of 9 months' duration. She had been perfectly well until September, 1939, when she had an acute sore throat. Three weeks later she developed high fever and migratory arthritis involving both ankles, knees and elbows and the temporomandibular joints. Two weeks after the onset of joint symptoms there was evidence of myocarditis and pericarditis. The patient was treated in another hospital and remained extremely ill for 8 months. Thereafter she improved steadily and apparently had no residual evidence of cardiac or joint damage. In October, 1940, a tonsillectomy was performed.

rowing and irregularity of the joint spaces. The electrocardiogram was normal.

The patient continued to improve and at discharge on March 31, 1942, was free of symptoms. Motions of the joints had improved. The sedimentation rate remained elevated but had fallen to normal 1 month later. The patient returned to school in September, 1942, and has remained free of symptoms ever since. The sedimentation rate has remained normal except for an elevation to 0.5 mm per minute on two occasions. The only residual changes in the joints are slight limitation of motion of both wrists and slight recession of the jaw. The heart is normal.

The acute onset three weeks after a sore throat, the migratory joint symptoms with relatively little swelling, redness or tenderness in the first attack and the involvement of the myocardium and peri-

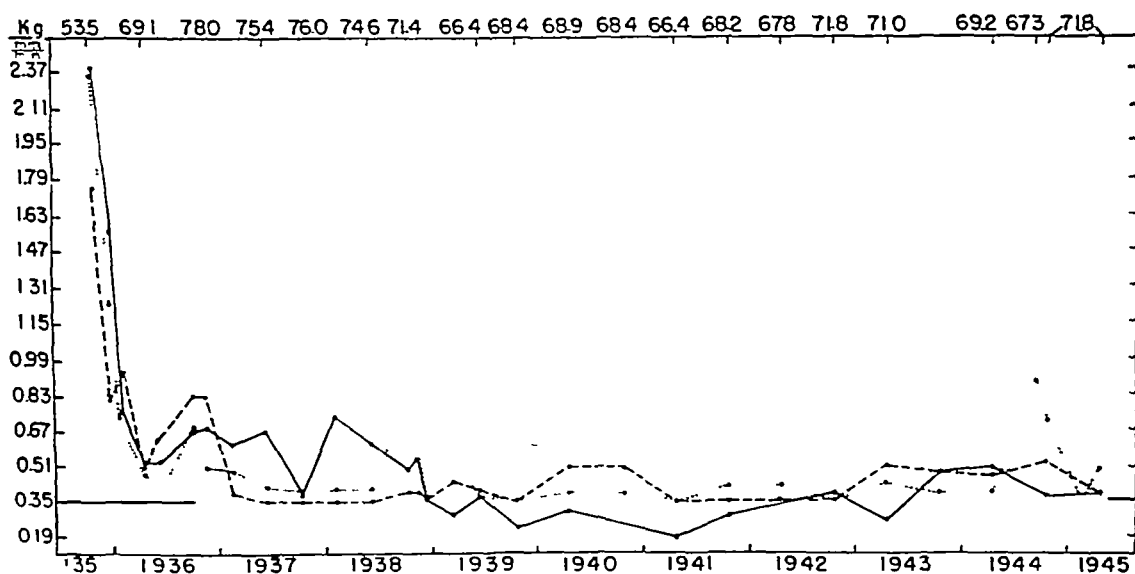


FIGURE 2 Graphic Presentation of the Course of the Disease in Case 3

The solid line represents the sedimentation rate, the dotted line the subjective symptoms, and the broken line the objective joint findings. The method of obtaining the subjective and objective figures was the same as that used for Figure 1. The heavy line at 0.35 mm per minute indicates the upper limit of normal for the sedimentation rate and forms the zero line for the subjective and objective findings. The body weights are recorded at the top of the figure.

She remained well, although on limited activity, until May, 1941, when she had recurrence of high fever, pain and swelling of many joints, especially the wrists and fingers, together with chest pain, dyspnea and orthopnea.

In July, 1941, the patient was admitted to another hospital. The only cardiac findings of significance were slight enlargement, a soft systolic murmur at the apex and a low T_1 in the electrocardiogram. There was no evidence of failure. She improved slowly and by November, 1941, the temperature had become normal, the corrected sedimentation rate began to fall from the original level of 1.5 mm per minute and she began to gain weight.

At the time of transfer to this hospital there was slight cardiac enlargement, but no murmurs were heard. Joint examination showed slight recession of the jaw and slight limitation of motion of the neck, shoulders and elbows. The periarticular tissues of both wrists were thickened, and motion on the right was limited to 5° of extension and 10° of flexion. The metatarsal heads were depressed and there was a cockup deformity of the toes. Routine laboratory examinations were normal except for a sedimentation rate of 0.5 mm per minute and a white-cell count of 19,000. There was x-ray evidence of slight cardiac enlargement to the right and left and dilatation of the left auricle. The wrists showed generalized decalcification of the bones, with several circumscribed areas of decreased density, and there was slight nar-

cardium were suggestive of rheumatic fever. The subsequent chronic involvement of joints with thickening of periarticular tissues and deformities and the x-ray evidence of decalcification of the bones around the joints and slight narrowing and irregularity of the articular spaces made it apparent that the correct diagnosis was rheumatoid arthritis. The high, spiking temperature, the extremely severe constitutional symptoms and the myocarditis and pericarditis are frequent manifestations of severe rheumatoid arthritis. During the first three years the disease remained active, although the partial remission for ten months gave evidence of the characteristic tendency to remit. Subsequently there was a complete remission, which has persisted through the past three years. Despite the severity of the disease, there are no residual joint findings except slight limitation of motion of the wrists and slight recession of the jaw, and there is no evidence

of cardiac abnormality. Slight retardation of growth often found in children with rheumatoid arthritis is apparent.

When the onset is monarticular, rheumatoid arthritis may resemble traumatic arthritis. Not uncommonly trauma is the precipitating factor that initiates the apparent onset of rheumatoid arthritis. In such cases attention is often focused on the injury, and to it is ascribed the subsequent joint involvement. If, however, joint symptoms do not appear for twelve hours or more after the injury or persist for months after uncomplicated trauma, one should hesitate to make a diagnosis of traumatic arthritis. In some cases evidence of involvement of other joints may be obtained by direct questioning as to each joint. Loss of weight, excessive fatigability or an increase in vasomotor symptoms constitutes further evidence against traumatic arthritis. Marked thickening of periarticular tissues, roentgenologic evidence of subchondral bone atrophy, elevation of the sedimentation rate and marked abnormalities in the synovial fluid suggest the presence of rheumatoid arthritis. In other patients, as in Case 5, such evidence is absent or overlooked and the correct diagnosis is not made until further progression of the disease has occurred.

CASE 5 A 23-year-old schoolteacher was admitted to the hospital on August 10, 1939, because of swelling and limitation of motion of the left knee of 1 year's duration. In August, 1938, her left knee locked in flexion when she squatted to pick up an object. The knee became swollen and stiff and only slowly returned to normal. Eight months later the swelling recurred without associated trauma and persisted to the time of admission. The past history was noncontributory.

Examination on admission showed an effusion in the left knee and tenderness in both tibiofemoral fossae and over the medial side of the joint. Routine blood and urine examinations were normal except for a white-cell count of 11,500 per cu mm.

A diagnosis of internal derangement of the knee was made and operation was performed on August 12. The synovial membrane was found to be thickened, and there was definite pannus formation in the region of the intercondylar notch. The cartilaginous surfaces of the joint seemed normal except in areas in which they were covered by pannus. The internal semilunar cartilage was hypermobile and was removed. Fluid aspirated at the time of operation contained 25,600 white cells per cubic millimeter, of which 96 per cent were polymorphonuclear leukocytes. The sugar content was 41 mg per 100 cc. Microscopic examination of synovial tissue removed at operation showed a chronic synovitis consistent with that found in rheumatoid arthritis. There were hypertrophy and villous overgrowth of the synovial tissue. In the subsynovial layers there was widespread marked cellular infiltration consisting chiefly of mononuclear cells.

Following the operation the left knee remained swollen and stiff. In November, 1939, the patient noticed increasing fatigability and the left ankle and foot became swollen and extremely painful. In December, the right knee, right hip and right ankle became involved. The fatigability and weakness persisted, and early in 1940 there was involvement of the neck, left shoulder, left elbow, both wrists and the first and second metacarpophalangeal joints bilaterally.

The patient was readmitted on June 21, 1940. On direct questioning she recalled that she had been fatigued and had lost 10 pounds during the winter of 1938-1939, when she had been under physical and emotional strain. On admission she was emaciated and had marked atrophy of muscles, especially around the left shoulder girdle. The 1st metacarpophalangeal and interphalangeal joints of both hands were red, swollen and painful. There were limitation of motion and swelling of both wrists and both knees and only a few degrees of motion of the left shoulder in any direction. Routine blood and urine examinations were not remarkable. The corrected sedimentation rate was 0.78 mm per minute.

On a regime of bed rest, exercises, hot packs to the left shoulder and both knees, aspirin, phenobarbital and discussion of emotional problems the patient steadily improved. She was discharged on July 24.

In this case, the operation, which was undertaken on the assumption that the patient had internal derangement of the knee, precipitated a more generalized stage of the disease. The synovial-fluid findings, with high white-cell and polymorphonuclear leukocyte counts and a low sugar content, were entirely inconsistent with those of traumatic effusions. If obtained preoperatively, they would have suggested the correct diagnosis and operation would not have been performed. The operative findings, the microscopic examination of the tissue and the subsequent course made it apparent that the patient had rheumatoid arthritis.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31461

PRESENTATION OF CASE

A forty-two-year-old woman entered the hospital in coma.

Five months before admission in another hospital, she had undergone a right radical mastectomy for a malignant tumor. After the operation she received twenty courses of x-ray treatment over the operative site, the total dosage being 4800 r. The last irradiation had been given six weeks before admission. She felt well until several weeks before admission, when anorexia and gradually increasing weakness developed. At about the same time she began to complain of pain low in the back, which radiated down the right leg, with a sensation of numbness. Five days before admission she had a chill and vomited once. On the afternoon before admission, she developed a nonproductive hacking cough and a pink maculopapular rash broke out over the entire body. She became increasingly restless, and on the morning of the day of admission she was found in coma.

She had had spasticity of the right side of the body since birth. A chest film two months before admission showed clear lung fields with some coarsening of the markings.

Physical examination revealed the patient to be poorly nourished, cyanotic and in coma. The skin was hot and moist, and a rash consisting of papules with petechial centers was seen over the body, especially over the ankles and forearms. The eyes were wandering. The pupils were regular and equal and reacted to light. The mouth was opened with difficulty, and the pharynx was seen to be markedly injected. The neck was stiff but not more so than it usually was. A spastic palsy was present on the right side, with athetoid movements of the right hand, a right pes cavus and a dorsal scoliosis to the left. The right leg was shorter than the left. A right mastectomy scar was present. The skin was pigmented in this area. The heart was normal. The lungs were hyper-resonant, with tympany over the left upper lobe. There were no rales. The trachea was deviated to the left. The abdomen was normal. The reflexes could not be elicited.

*On leave of absence

The temperature was 102°F, the pulse 140, and the respirations 32. The blood pressure was 108 systolic, 56 diastolic.

Examination of the blood showed a red-cell count of 3,580,000, with 8.9 gm of hemoglobin. The white-cell count was 12,800, with 39 per cent neutrophils, 54 per cent lymphocytes and 7 per cent monocytes. The urine gave a ++ test for albumin, and the sediment contained frequent hyaline casts, a rare red cell and an occasional white cell.

A chest film taken with a portable machine soon after admission showed granular, diffuse areas of increased density through which open bronchi could be traced, extending from each hilus outward to occupy the greater portion of each lung, apparently sparing only the lung tissue in the left lower chest and in the right apex (Fig. 1). There was no fluid in the pleural sinuses. The heart was somewhat enlarged. The hilar vessels could not be made out. Lumbar puncture revealed clear colorless fluid under an initial pressure equivalent to 160 mm. of water. The cell count was 1 polymorphonuclear cell and no red cells per cubic millimeter. The total protein was 19 mg. per 100 cc. Blood and throat cultures were negative.

Twenty thousand units of penicillin was given every three hours intramuscularly. Later adrenocortical extract and 5 gm. of sodium sulfadiazine in 5 per cent dextrose in saline were administered. The patient's blood pressure fell steadily and she died twelve hours after admission.

DIFFERENTIAL DIAGNOSIS

DR. J. H. MEANS: One might say that this story separates itself into separate chapters. Five months before death this patient had a radical mastectomy for malignant disease of the breast, which I suppose was a carcinoma. Evidently they thought that it was a highly malignant one because they gave heavy radiation therapy after mastectomy. I do not know what interpretation to put on that with regard to whether or not the surgeon thought he got it all out. I gather that he did not think so. I asked one of our cancer experts about the policy here regarding radiation, and apparently there is a difference of opinion. Some men are inclined to give x-ray treatment in all such cases, whereas others do not do so unless they are quite apprehensive about recurrence, as for example when the axillary lymph nodes are involved. She did well for several weeks before admission, having apparently got through the mastectomy and heavy radiation therapy without much trouble. She then developed symptoms that consisted of anorexia and weakness, which are symptoms of so many things that one cannot interpret them. Then with the pain low in the back and the numbness in the right leg, one wonders whether she was developing metastatic disease in the spine.

The last chapter of this story seems to be an extremely acute affair which began with a chill,

vomiting, a hacking cough and a maculopapular rash, which later became petechial. Her illness became productive of coma on the fifth day, and she died on the sixth day. It must have been an extremely fulminating infection.

Frankly, I find this a difficult problem, and I do not know what the answer is, but one has certain obvious lines of approach. In the first place, is there a possibility of explaining the whole picture on the basis of malignant disease? If possible, we like to

illness characterized by? Chills and the onset of a rapidly progressive maculopapular rash. I did not see this rash, but I probably should not have known any more about how to interpret it if I had.

I cannot explain everything on the basis of cancer, but I can explain a number of things on that basis. Usually if one works hard to explain everything in the record, it turns out that some of the things are fakes. But I suppose the rash here described was really present. I wonder if a general carcinomatosis



FIGURE 1 *Roentgenogram of Chest*

explain the whole story on the basis of one diagnosis. Some people do have more than one disease though, and if one tries too hard to make everything fit one etiologic diagnosis one may come to grief. Except for a desire to connect the cancer with the terminal events, one would say that the terminal events were due to some sort of fulminating infection. There seems to be enough evidence suggesting infection to make one take that as one's first choice. Evidently the doctors in charge thought that infection might have been present, because they gave both penicillin and sulfadiazine, neither of which stopped the downhill course. What was the last

can produce a picture such as this, with cerebral, spinal and pulmonary metastatic disease. The fever is difficult to explain on the basis of cancer. The patient ended up in coma, also in shock. One wonders about that, and one notices that they gave adrenocortical extract. Did this patient's adrenal glands give out toward the end? They may well have, but there are various ways in which they may fail. They may fail in an infection of an overwhelming sort. I toyed with the remote possibility of involvement of both adrenal glands in a metastatic malignant process. I do not believe that this occurred, but it should be mentioned in an elaborate

differential diagnosis I shall not say any more about the possibilities of malignancy because I really think that the patient had a superimposed terminal infection.

Another possible line of thought is that a non-malignant cerebral accident put her into coma. One has to think of all the possible causes of coma. This patient was never uremic, so far as I can make out on the data presented. One does not know the non-protein nitrogen, however. Was it done?

DR HELEN S. PITTMAN: No, everyone thought that someone else had taken it.

DR MEANS: Probably some kind of nephritis was found, but that is not the important picture. Nothing is said about the smell of the breath or anything of that sort, and I hesitate to make a diagnosis of uremia. She was not diabetic. She had not had a head injury. I do not believe that a cerebral accident would produce a fever of this sort. Embolus to the brain, cerebral hemorrhage, cerebral infarction and encephalitis do not seem to fit. There is no evidence of meningitis. The lumbar puncture was negative, and the neck was not stiffer than it always had been. Nothing is said about a Kernig sign. I cannot make a diagnosis of any kind of meningitis, although the rash may have been due to a meningococcal infection, which can produce a rash of this kind. I cannot go any farther with the intracranial situation or the causes of coma. I do recall that Dr Stanley Cobb once pointed out that if a cerebral lesion is not productive of many symptoms and then an infection is superimposed, you could get all sorts of bizarre symptomatology. If she had something noninfectious in the head and then got an overwhelming infection, it might have produced this rapid development of coma.

Let us now work on the infectious part of the story. We have a little evidence pointing to the lung. The physical signs in the chest were queer. Of course, we should clear up the old business of birth injury, which comes in to confuse the picture with regard to the neurologic examination. I gather that she had old birth palsy, with shortening of the right leg and scoliosis. I wonder whether the deviation of the trachea had anything to do with the deformity of the chest. I shall call on the radiologist for help in a moment. Once in a great while one learns more by physical findings than the radiologist does by his technic, but that is unusual. Now these lung signs,—the hyper-resonance all over, the tympany in the left upper lobe, the absence of rales, the deviation of the trachea to the left and the loud harsh breath sounds,—about all I can get out of them is that it seems as if something was going on in the left upper lobe. Of course the deviation of the trachea makes one think that there was something pushing or pulling it over. If it was being pulled over, one would think of collapse, but if the lung was collapsed, I do not believe that one would expect to get harsh breathing. It is possible, I sup-

pose, if the bronchus was open. I shall reserve final opinion on that until I have seen what the radiologist can do for me.

DR CLAYTON H. HALE: It is difficult to explain the hyper-resonance in the chest from these films. I presume that there might have been some at the extreme right apex.

DR MEANS: The tympany was at the left apex, over the left upper lobe, and that portion of the film is duller than the other. It does not make sense.

DR HALE: I believe that there is some aeration, at least in the left lower lobe. I can see part of the left half of the diaphragm laterally, but the heart shadow obscures the remainder. This is a diffuse granular density. The upper and lower lobe bronchi on the right are demonstrated quite nicely, and thus we know that they are open. Here you can see a small horizontal shadow that appears to be the upper border of the middle lobe. Separating this from the density above suggests a circumscribed shadow that might be a metastatic mass in the right upper lobe. The trachea is in normal position. The heart looks large on these films, but they were made with a portable machine. I believe that one has to think of malignant disease and possibly superimposed consolidation in the other areas. I should not expect pulmonary edema to give a sharply demarcated area like this. I see no evidence of metastases to the bones and no collapse of any of the lobes.

DR MEANS: There was no collapse, and no fluid in the chest. We can forget the deviation of the trachea for the present. I must confess that by the x-ray studies I am more intrigued with my interpretation that a good deal of this picture might have been due to cancer than I was before I saw the films. It could have been a metastatic malignant lesion in the chest, and if it was in the chest it might also have been in the head. I think that I shall rest my case on a statement something like the following: The patient originally had a carcinoma of the breast, and she then developed the picture of rather widespread metastatic carcinoma. There is no x-ray evidence that it involved the spine. Is that an adequate roentgenologic study to exclude the spine?

DR HALE: No.

DR MEANS: Then I do not know whether or not she had it in the spine, but the history suggests that she may have. She had it in the lung and probably in the brain. I think that she had an old cerebral lesion, presumably due to birth injury, and that might turn up in the way of anything that the pathologist can find. She may have had a terminal infection of some sort. It could have been an overwhelming meningococcal infection or, of course, a streptococcal infection. I wonder if she could have had a rapidly progressing subacute endocarditis. She may have, but I do not see how one can make the diagnosis. I am simply going to let it go as a terminal infection of some kind. There may have

been a pneumonitis mixed up with this picture, but how much of the pulmonary lesion was due to pneumonitis and how much to cancer, I cannot say I shall have to let it go at that

DR PITTMAN I am glad that Dr Means could not make a diagnosis either Dr E L Young operated, because of the spasticity from the birth injury he was unable to abduct the arm sufficiently to get at the field, and he thought that he had not done an adequate axillary dissection For this reason, extensive irradiation was given

DR MEANS Speaking of irradiation, I thought of the possibility of pulmonary fibrosis resulting from irradiation, but that would only be directly under the operative site and would not explain such a widespread lung lesion

DR PITTMAN She had this episode of chills and vomiting, and five days later, when she was found unconscious, Dr Young was called He made a diagnosis of intracranial metastases and had her sent to Dr W J Mixter When Dr Mixter obtained normal spinal fluid under normal pressure, he decided that there was nothing in the head and asked me to see her At that time she had quite an insignificant skin rash, but it progressed rapidly during the course of the afternoon She entered the hospital with signs that I interpreted clinically as indicative of spontaneous pneumothorax She then developed pulmonary edema Dr Gardella, the resident, suggested that she had a meningococcemia, with the Waterhouse-Friderichsen syndrome I had not thought of that, but it seemed a reasonable diagnosis Dr Mixter, who had seen a number of cases in World War I, agreed, and from that point on the problem was therapeutic She came out of the pulmonary edema but nevertheless went into shock She was obviously moribund before getting what was, perhaps, overzealous therapy

DR MEANS I had not thought of the possibility of her dying because of so much intravenous therapy Is that what you are implying?

DR PITTMAN She was dying anyway The therapy may have produced the anatomic picture of pulmonary edema

CLINICAL DIAGNOSIS

Meningitis

DR MEANS'S DIAGNOSES

Metastatic cancer of lungs, probably brain and possibly spine

Terminal infection (type undetermined)

ANATOMICAL DIAGNOSES

Radiation pneumonitis

Papular rash

Scar right mastectomy

PATHOLOGICAL DISCUSSION

DR RONALD C SNIFFEN At the time of death this patient showed the deformities described in the clinical history There was a papular rash over all extremities, most pronounced on the flexor surfaces A few papules were scattered over the anterior chest, and a few macules over the abdomen no petechiae could be found The right mastectomy wound was well healed, and there were no signs of local recurrence There was slight tanning of the skin in this region Each pleural cavity contained approximately 150 cc of clear, straw-colored fluid, and each lung weighed 900 gm, which is about three times the normal weight This increase in weight was largely accounted for by a profound pulmonary edema There were no pleural adhesions or thickening No other gross abnormalities were found The heart was entirely negative The adrenal glands merely showed medullary autolysis, no metastatic cancer being detected A blood culture grew only colon bacilli

The important microscopic findings were confined to the lungs, and they are of interest In general there was a severe pulmonary edema, but all sections showed additional abnormalities The cells lining the alveoli and atria had increased tremendously in size (Fig 2) Many showed extreme hypertrophy and distortion and were gradually desquamating into the alveolar spaces, a few of these cells were multinucleated Many of the alveoli contained a thick homogeneous hyaline membrane, which was closely applied to the alveolar wall or was slightly lifted from it The alveolar walls were hyperemic and edematous, the endothelial and septal cells were swollen, and the elastic fibrils were thickened and fragmented

No one of these pulmonary changes is peculiar to any one condition, but in this combination they are said to be characteristic of radiation pneumonitis Warren and Gates^{1,2}, and Warren and Spencer³ have reported these reactions in detail from a study of autopsy material and have produced them experimentally in various animals by means of radiation

DR MEANS What was the round mass in the chest that the radiologist talked about?

DR SNIFFEN We did not find a mass Severe pulmonary edema was the only gross abnormality

DR HALE Were these microscopic changes present in the left lung?

DR SNIFFEN Unfortunately our sections were not taken with reference to the field of radiation, but all of them showed the same abnormalities and blocks of tissue were taken from each lung

DR CHARLES S KUBIK It is not often that we have a chance to observe the pathologic lesions of infantile hemiplegia so many years after its onset The left cerebral hemisphere was considerably smaller than the right The left cerebral peduncle was extremely small, owing to secondary degeneration

tion of the corticospinal tract. The original lesion was probably in the left lenticular nucleus and internal capsule, nearly all the lenticular nucleus was destroyed, and the degeneration of the cortico-

Evidently even the pathologists do not know the cause of death.

DR SNIFFEN: I believe that the radiation pneumonitis was the major contributing factor. We

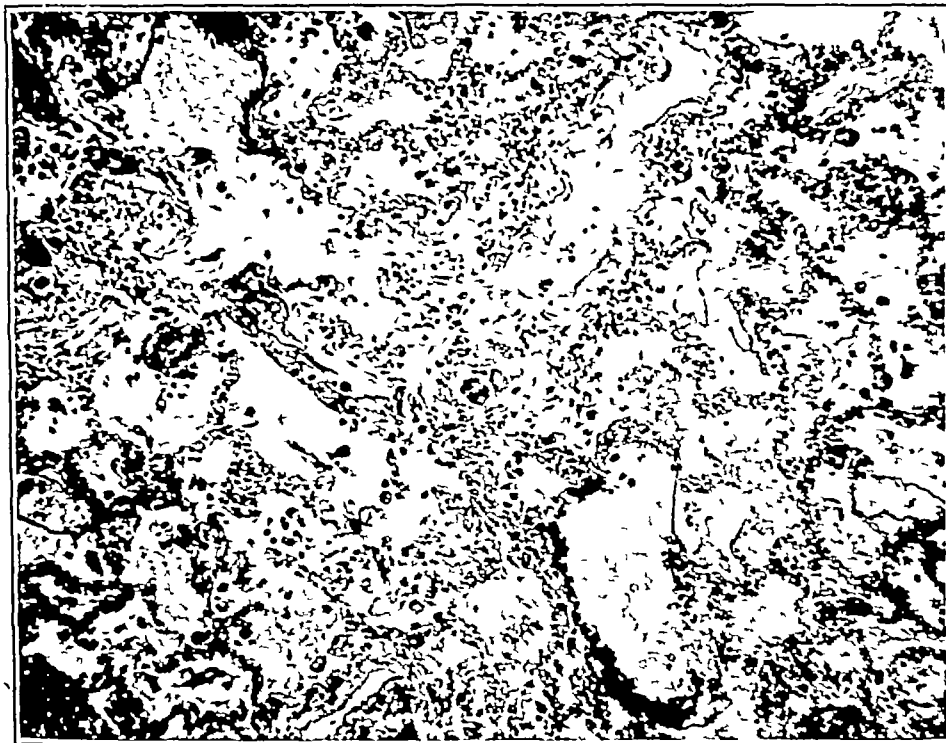


FIGURE 2. Photomicrograph of Lung

spinal tract was unquestionably due to involvement of the internal capsule by the lesion. There was no residual softening, cavitation or discoloration but, so far as one could tell, only a loss of substance. The nature of the original lesion is not clear. I suppose that it was acquired, not developmental, and it may have resulted from a birth injury.

DR MEANS: I feel reconciled about this case.

were unable to find evidence of a superimposed fulminating infection.

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CASE 31462

PRESENTATION OF CASE

A fourteen-year-old boy entered the hospital complaining of pain in the right small toe.

Five months before admission the patient first noticed that walking or direct pressure to the toe caused sharp pain. Immersion in cold water also caused pain. There was no history of previous trauma. He was seen in the Out Patient Department three months before admission, where examination showed tenderness and redness but no limitation in motion. The impression was that the soft-tissue swelling was due to a tight shoe. He was

seen in the Out Patient Department a few times during the next two months. X-ray studies showed an area of rarefaction involving the terminal phalanx of the right fifth toe. There was no definite periosteal proliferation. Soft-tissue swelling was considerable. Removal of the toe was advised.

On admission, physical examination was negative except for marked swelling of the right small toe, which was enlarged to twice its normal size. It was especially tender on the dorsal surface but not red or warm beneath the nail. A blister was present on the plantar aspect. Motion of the toe was limited.

Examination of the urine and blood was negative. A blood Hinton test was negative. The blood uric acid was 6.2 mg per 100 cc (normal).

X-ray films of the toe showed somewhat more decalcification of the terminal portion of the distal phalanx than was seen previously. The periosteal outline was preserved, and in the center of the decalcification there was a dense area (Fig 1). An x-ray film of the spine was negative.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR JOHN REIDY: We might begin by looking at the x-ray films.

DR CLAYTON H. HALE: This film shows the soft-tissue swelling that was described and the decalcification of the distal half of the terminal phalanx.



FIGURE 1 Roentgenogram of Terminal Phalanx of Fifth Toe

fication of the distal half of the terminal phalanx. A film taken some two months later shows extension of the decalcification. I can make out no periosteal reaction. I cannot tell whether the soft-tissue swelling is arising from the phalanx or the surrounding soft tissue.

DR REIDY: Is there anything circumscribed about it, or is it generalized decalcification?

DR HALE: It extends to the junction of the proximal and middle thirds, where there is a rather abrupt transition from normal to decalcified bone.

DR REIDY: It chiefly involves the terminal portion of the phalanx.

DR HALE: On this other film you can see the junction of the decalcified area with the supposedly normal bone, and I presume that this is the dense island described in the center of the decalcified area.

DR REIDY: What would you take the dense spot to be—new-bone formation or the remains of the old shaft?

DR HALE: It seems likelier that it represents the remains of the old shaft, but it is difficult to tell. It is surrounded by decalcified bone.

DR REIDY: In a fourteen-year-old boy with these symptoms one would consider first of all, as they did in the Out Patient Department, pressure due to tight shoes. If that had been the case, however, I am sure that he would have been relieved.

This apparently was a destructive type of lesion, yet there is no evidence of periosteal proliferation, which I believe is more or less against its being an infectious process, either of pyogenic or tuberculous origin. The negative laboratory studies, that is, those of the blood and the urine, are also against its being an inflammatory process. The fact that he had a blister on the plantar surface of the toe suggests that this might have been the point of entrance of an infection. Yet the blister was present five months after the onset of the original symptoms, so I doubt that it played any part in the primary process. It was likelier the result of the marked swelling rather than the cause of it. Tuberculosis or a low-grade inflammatory process should be considered. Yet, here again there should have been some evidence of regeneration of bone if it had gone on for this length of time, although probably less than what would have been present with a pyogenic type of infection. There is no mention of a tuberculin test. Apparently they were not considering this possibility. There is no evidence of tuberculosis elsewhere in the body, so I believe that tuberculosis was probably not the cause of the difficulty.

The fact that x-ray films were taken of the lumbar spine suggests a neurotrophic lesion, that is, something that had resulted from a spina bifida or a nerve-root irritation. This type of lesion is usually associated with an inflammatory reaction, and usually there is no pain. The facts that he had pain and no evidence of periosteal proliferation and that the x-ray films of the spine were negative make me believe that a neurotrophic disturbance was probably not responsible for his difficulty.

Gout should be thought of, since we know that it will produce lesions in the bones and joints. To have a single lesion in a fourteen-year-old boy would be most unusual. Furthermore, there is no other evidence of bone or joint difficulty, and the blood uric acid level was normal. Therefore I do not suspect gout too seriously.

The other things that one might consider are enchondroma of bone. This would probably give

a much more clear-cut picture than we have here. Although enchondroma does occur in the terminal phalanx it rarely ever causes pain unless there is a fracture through it. Do you think there is any evidence of this, Dr Hale?

DR HALE: I cannot see a fracture.

DR REIDY: If the bone had been fractured, it would have healed fairly promptly and the symptoms would have been relieved. The same reasoning probably holds true for xanthoma or any kind of cystic bone disease. The symptoms are not

since he continued to complain of it over this period of time. I believe that the picture best fits into the so-called "glomus-tumor" syndrome, a condition in which the tumor arises from the connecting mechanism between the terminal arteriole and primary venule and may cause bone destruction by direct pressure. This causes severe pain, and is not unusual in the subungual area. I have seen the thumb involved several times. I do not recall having seen one in the foot, but the character of the pain and the lack of any other diagnostic feature

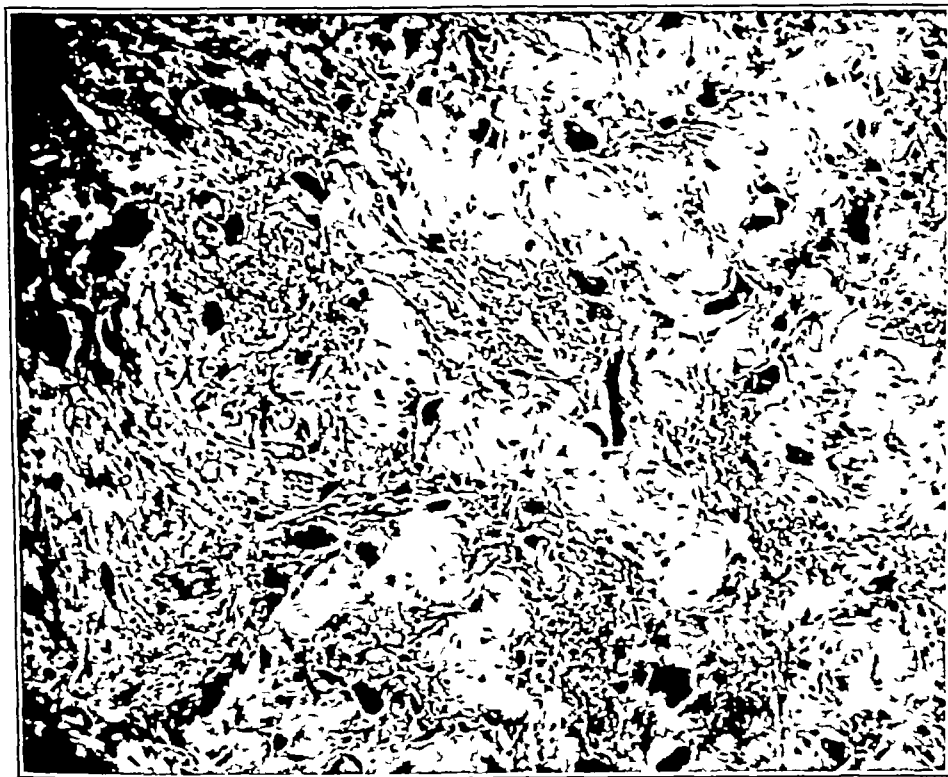


FIGURE 2 Photomicrograph of Nidus in Terminal Phalanx of Fifth Toe

marked unless something in the way of injury occurs. These conditions are susceptible to injury because of the weakened bone. A subungual exostosis can occasionally cause considerable discomfort, but it would not produce this type of picture, even with the atrophy of disuse that goes with it. If he had pain to that extent, there would be decalcification in the remaining toes, as well as in the terminal phalanx of the fifth toe. A so-called "subungual melanoma" might be considered, but in five months one certainly would expect much more evidence of destruction and complete discoloration and probably some breaking down of the tissues.

The type of pain is consistent with a neurovascular lesion. The pain was aggravated by changes in temperature and apparently was fairly severe,

certainly suggest a glomus tumor as a good possibility. The only thing against a glomus tumor is the fact that there was no evidence of discoloration beneath the nail, which is usually present. I believe, however, that this fills the bill better than any other lesion that I can think of, and I shall make a diagnosis of glomus tumor of the terminal phalanx of the right fifth toe.

CLINICAL DIAGNOSIS

Glomus tumor of terminal phalanx of right fifth toe

DR REIDY'S DIAGNOSIS

Glomus tumor of terminal phalanx of right fifth toe.

ANATOMICAL DIAGNOSIS

Osteoid osteoma of terminal phalanx of right fifth toe

PATHOLOGICAL DISCUSSION

DR RONALD C SNIFFEN When the terminal phalanx was split longitudinally one could see an injected, firm, circumscribed area approximately 5 mm in diameter in the distal tip. This nidus lay in the medulla and had not broken through the cortex.

Microscopically the nodule showed a background of vascular connective tissue in which trabeculae of osteoid were embedded, and these were lined by osteoblasts and, at some points, by osteoclasts. Occasionally the osteoid seemed to be undergoing

calcification (Fig 2). The trabeculae of the adjacent spongy bone were somewhat thickened.

There was no inflammatory infiltration in the bone, nor evidence of degeneration. Our diagnosis was osteoid osteoma. Apparently the small nidus had produced quite a severe reaction around it as a consequence of repeated trauma. This is the first osteoid osteoma we have seen in this region. Jaffe and Lichtenstein* have reported several cases in which the lesion arose in the pedal phalanges.

Dr Hale, with the knowledge that this is an osteoid osteoma, can you see the nidus in the roentgenogram?

DR HALE The 2-mm area of increased bone density surrounded by decalcified bone probably represents the nidus of osteoid osteoma.

*Jaffe, H. L. and Lichtenstein, L. Osteoid-osteoma: further experience with this benign tumor of bone. *J. Bone & Joint Surg.* 22: 645-682, 1940.

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SAFE AND SANE FOURTH

MANY thoughtful persons have come to the conclusion, in recent years, that war as a major calamity ranks second only to that greatest human calamity of all — man's inhumanity to man, of which war, after all, is only an organized expression. And yet nations that are, on the whole, peace loving so long as they can have their own way occasionally enter into war if the provocation or the danger that is pressing seems great enough.

To measure the losses and the gains after the deed is a chastening experience. The main goal may have been won, but goals are often illusive, and the cost is always excessive. It would be folly to attempt now to run a trial balance on the tangled affairs of the last four or five years, we can only say that we have saved ourselves from immediate oblivion,

whatever the cost. Whether we can ever pay this immediate cost or, indeed, the continuing and mounting cost of man's inhumanity to man is another matter.

Aside from the main decisions that are now being contested among the winners themselves, some slight benefits may be checked against the losses in material, in lives and portions of lives and in moral values. There is no denying that technology has made great advances both in destruction and in its antidotes, and many of these discoveries can be directed toward peacetime uses. Even atomic energy, about which we are now becoming almost blasé, will revolutionize industry and life itself, they say, if life survives the experiment. Medicine and surgery, as always, gain impetus through the need of saving life and limb in time of war. For those that are tough enough not to be consumed by it, the crucible of war may be a refining agent, just as the experience of working in a common cause against a common danger is an uplifting one if its beneficiaries can overcome the demoralizing effect of release from that danger, labor gains in importance and earns higher rewards each time it becomes a partner in any important enterprise, and its benefits will become lasting in proportion to its ability to appreciate the mutuality of its partnership.

It was, however, the safe-and-sane Fourth of July on which we had planned to comment. Designed and enforced as a war measure to conserve ammunition and keep our powder dry, its continuance in the halcyon days of peace will signalize a real and revolutionary step in the progress of civilization. A race that has learned in time of war to respect the agents of destruction in times of peace has certainly something to add to the credit side of the ledger.

ALBRECHT DÜRER AND ANATOMY

ALTHOUGH Dürer is widely recognized as the father of copper-plate engraving for book illustrations and also as one of the great painters of his age, his work on anatomy, particularly in relation to the proportions of the human body, is less well known. He began to be interested in this subject early in his life. Apprenticed at the age of fifteen to Michael

Wohlgemuth, the foremost wood engraver of his day, Dürer had the best of training. After seven years he was sent by his father on an extended trip throughout Europe, and it was in Italy, just before the turn of the sixteenth century, that he caught the significance of picture printing in contrast to book printing, which by that time was firmly established, with the presses pouring out incunabula in considerable number. Dürer visualized the propagation of thought by the use of pictures, and since he was essentially an artist, he studied in particular the delineation of the human figure.

Returning to his native Nürnberg, he soon became intimate with such humanists as Hartmann Schedel and Willibald Pirckheimer, and it was during the years just after 1500 that Dürer made his great series of copper engravings, including *Melancholia*, so well known to physicians, as an expression of intellectual research. About 1528 he painted *The Four Apostles*, his highest achievement in art.

His book *On Human Proportions* occupied many years of his life but was not published until just after his death in 1528. The first edition, in German, contains superb engravings showing the surface anatomy, with particular attention to studies of the various proportions of the body. Dürer drew not only figures of persons of various size and shape but also infants and a few suffering from diseases that had deformed their stature. It is from this book that most subsequent studies in art anatomy have developed, and the illustrations, drawn so exquisitely by Dürer, are frequently reproduced in textbooks of the present day. Apparently the German edition of 1528 was not widely disseminated, for it was not until the book was translated into Latin, the language of the scholar, in 1532-1534 that Dürer's famous work became widely known. Additional translations into French, Italian, Portuguese and

Dutch were made within a few years. The edition of 1528 is a rare book, and all the early publications are not by any means plentiful. Few men, by one publication, have exerted a wider influence.

NOTICES

NEW ENGLAND HEART ASSOCIATION

A meeting of the New England Heart Association will be held in the Boston Medical Library on Monday, November 26, at 8:15 p.m.

PROGRAM

The Use of Cytochrome C in Combating Tissue Anoxia. Dr. Samuel Procter

Testosterone Propionate Therapy in 100 Cases of Angina Pectoris. Dr. Maurice A. Lesser

Surgical Treatment for Coarctation of the Aorta. Dr. Robert Gross

Venous Catheterization in Patients with Congenital Heart Disease. Drs. C. Sidney Burwell and Lewis Dexter

Experiences during the Past Year at the Massachusetts General Hospital in the Dietetic Treatment of Congestive Heart Failure. Drs. William C. Bridges, Edwin Wheeler, and Paul D. White

MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to

George L. Schadt, Chairman
Postwar Loan Fund
8 Fenway
Boston 15, Massachusetts

Interested physicians and medical students are cordially invited to attend.

SOUTH END MEDICAL CLUB

The next meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, November 20, at twelve noon. Dr. Thomas J. Anglem will speak on the subject "Thiouracil in the Treatment of Thyroid Disease." Dr. Frederick J. Simmonds will preside.

Physicians are cordially invited to attend.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, NOVEMBER 22

FRIDAY, NOVEMBER 23

- *1 10:00-10:00 a.m. Some Aspects of Penicillin Therapy. Dr. Maxwell Finland. Joseph H. Pratt Diagnostic Hospital
- *2 10:00-10:00 a.m. Medical clinic. Isolation Amphitheater. Children's Hospital
- 10:30 a.m. Dermatology and syphilology. Amphitheater. Dowling Building. Boston City Hospital

SATURDAY, NOVEMBER 24

- *10:00 a.m.-12:00 p.m. Medical staff rounds. Peter Bent Brigham Hospital

MONDAY, NOVEMBER 26

- *12:00 p.m.-1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital
- *8:15 p.m. New England Heart Association. Boston Medical Library

(Notices continued on page xxvii)

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DERMATOME SKIN GRAFTS FOR BURNS IN PATIENTS PREPARED WITH DRY DRESSINGS AND WITH AND WITHOUT PENICILLIN*

STANLEY M. LEVENSON, M.D.,† AND CHARLES C. LUND, M.D.‡

WITH THE TECHNICAL ASSISTANCE OF MARION E. LAMB,§ AND ALICE K. DALY||

BOSTON

SUCCESSFUL skin grafting is necessary for the rehabilitation of the patient with extensive burns of the full thickness of the skin. Among the important factors essential to success are the following: First, the general and nutritional condition of the patient must be sufficiently good so that cells and blood vessels can grow¹; second, contact of the graft with the bed of granulations must be maintained²; and third, infection must be controlled, since in the presence of virulent infection grafts do not live³. Although cellulitis, lymphangitis and other evidences of spreading infection are infrequent under the present modes of therapy,^{4,5} all granulating third-degree burns are locally infected, and grafting must be done in the presence of some infection.⁶ Many measures have been used in the past in an attempt to minimize the deleterious effects of the local infection, thus, frequently changed dressings moistened with saline or Dakin's solution have been recommended.

Hirschfeld et al.³ have recently reported on the results of skin grafting at the Detroit Receiving Hospital. They state that, prior to the study, loss of 25 per cent or more of the grafted skin occurred in about a third of the cases. These failures were ascribed to the presence of infection. To attempt more effective control of this factor, penicillin was given by the intramuscular route in hourly doses of 5000 units, beginning twelve hours before

operation and continuing until the first postoperative dressing change. There were no demonstrable changes in the cultures of the granulating areas under the penicillin treatment, but the takes of the grafts were consistently good and in marked contrast to previous experience. The improvement was ascribed to the probable bacteriostatic effect of penicillin.

Until March, 1944, the results of skin grafting at the Boston City Hospital were similar to the earlier results reported by Hirschfeld; that is, in about one third of the cases there was less than seventy-five per cent take and in many of these cases the failure was 100 per cent. It was therefore decided to try the use of parenteral penicillin.

METHODS

From March to September, 1944, 28 Padgett-dermatome⁷ grafts were done on 19 patients with granulating third-degree burns, all of whom were in reasonably good general condition at the time of grafting. Until the time of the present study it had been customary, as in many other clinics, to use frequently changed wet dressings—usually saline or Dakin's solution—preparatory to grafting. It was believed that this treatment afforded so many opportunities for new bacterial contamination at each dressing that any bacteriologic studies would be difficult of interpretation. Consequently, the dressings in all the present cases before and after grafting were dry sterile pressure dressings with adequate splinting. These were changed at intervals of one to three weeks in the preoperative period. The first postoperative dressing was usually done about the sixth day. Aerobic cultures were taken from the granulating areas at dressing changes. No routine anaerobic studies were made. In 14 grafts preoperative and postoperative penicillin was given intramuscularly in doses of 15,000 units every three hours, usually begun one to two days prior to grafting and continued until the first

*From the Burn Assignment of the Surgical Services, the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard) and the Mallory Institute of Pathology, Boston City Hospital, and the Department of Surgery and the Department of Medicine, Harvard Medical School.

The work described in this paper was done under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University.

The penicillin used in this study was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for clinical investigation recommended by the Committee on Chemotherapeutic and Other Agents, National Research Council.

†Research associate in surgery, Boston City Hospital; research fellow in medicine, Thorndike Memorial Laboratory, Boston City Hospital; research fellow in medicine, Harvard Medical School.

‡Visiting surgeon, Boston City Hospital; assistant professor of surgery, Harvard Medical School.

§Bacteriologist, Mallory Institute of Pathology, Boston City Hospital.

||Assistant bacteriologist, Mallory Institute of Pathology, Boston City Hospital.

dressing change after the operation. No penicillin was used locally. In the other 14 grafts, no penicillin or other chemotherapeutic agents were given during this time. Four of the latter patients had

of a small portion of the graft occurred at the edges, but there was no loss of any central area. In the 80 to 90 per cent takes there was some loss of grafted skin in the central areas, as well as losses at the

TABLE 1 Summary of Data concerning 28 Dermatome Skin Grafts in Patients Treated with and without Penicillin

CASE No	AGE	SEX	AREA OF BODY SURFACE BURNED		NO OF PREVIOUS GRAFTS	PERIOD FROM BURN TO GRAFT	AREA OF BODY SURFACE GRAFTED		SITE OF GRAFT	HEMOGLOBIN	PLASMA PROTEIN	TAKE OF GRAFT
			Total	Third-degree			%	%				
	yr		%	%		days				%	gm/100 cc	%
1	2½	M	20	15	1	89	2	Chest	94	7.6	100	
2	38	F	40	20	0	51	6	Arm	82	5.4	95	
3	58	F	15	10	3	109	5	Arm	94	5.9	90	
4	5	F	10	8	0	37	8	Chest and axilla	85	5.7	100	
5	32	M	7	2	2	65	2	Arm	102	6.2	85	
6	40	M	5	2	0	67	2	Leg	90	6.2	90	
7	48	M	20	15	0	63	3	Arm	63	6.6	100	
8	45	M	20	12	0	118	5	Legs	84	5.4	95	
9*	1½	F	2	2	3*	200	2	Arm	76	6.8	95	
10	10	M	15	10	1	116	5	Leg	88	7.5	100	
11	6	M	10	8	1	75	3	Leg	87	5.7	95	
12	42	F	15	10	0	49	3	Chest and flank	78	6.4	95	
13	75	M	20	6	1	111	3	Back	81	6.6	100	
13	75	M	20	6	2	120	2	Back	81	5.8	100	
2	38	F	40	20	2	80	5	Buttock and thigh	86	5.8	85	
3	58	F	15	10	4	126	4	Arm and breast	94	5.8	80	
7	48	M	20	15	1	72	6	Arm, back and chest	86	5.7	100	
7	48	M	20	15	2	162	3	Chest	85	5.5	95	
10	10	M	15	10	0	55	3	Leg	87	5.6	95	
11	6	M	10	8	0	44	5	Leg	84	6.6	100	
12	42	F	15	10	2	77	4	Buttock and flank	83	7.3	85	
13	75	M	20	6	0	24	1	Hands	63	5.1	100	
14	16	M	10	3	0	28	2	Thigh	88	6.2	95	
15	3	M	6	5	0	35	4	Leg	95	5.8	100	
16	45	M	20	15	3	153	3	Arm, chest and axilla	86	5.4	95	
17	30	M	1	1	0	44	1	Knee	95	6.4	95	
18	57	M	10	3	2	79	3	Leg	88	6.5	95	
19	83	F	5	2	0	86	2	Leg	76	5.4	100	

*At outside hospital, admitted to Boston City Hospital 190 days after burn.

†Culture was overgrown by *P. vulgaris* and no other organism was recovered.

‡Culture was overgrown by *P. vulgaris* and no gram positive organisms were recovered.

received penicillin earlier for previous skin grafting. At the time of grafting, granulation tissue was cut away when excessive, bleeding being controlled with warm saline packs. If the granulations were not exuberant, the surface exudate was wiped off with dry or saline sponges. All grafts were sewn in place.

RESULTS

The essential data are presented in Table 1. The over-all results of the grafts were approximately the same in both groups, as shown in Table 2. The takes in 11 of the 14 grafts in each group were 95 to 100 per cent, and those in the remaining 6 were 80 to 90 per cent. There was no case of less than eighty per cent take.

There was no essential difference between the 95 and 100 per cent results. In the former a loss

periphery. Some of these areas required small secondary grafts at a later date. For the purposes of discussion in the rest of this paper the 95 to 100

TABLE 2 Results of Grafts with and without Penicillin Treatment

TAKE OF GRAFT	PATIENT TREATED WITH PENICILLIN	PATIENT NOT TREATED WITH PENICILLIN
%		
100	6	5
95	5	6
90	2	0
85	1	2
80	0	1

per cent takes are considered together and are contrasted with those of 80 to 90 per cent.

Sex and Age

There was no significant difference between the patients in the two groups in regard to sex and age.

approximately two thirds of the patients in each group were males and one third were females
The ages varied from three to eighty-three years in the nonpenicillin-treated group, and from one

Time of Grafting
The median time of grafting in the penicillin-treated group was eighty-two days after the burn, and that in the nonpenicillin-treated group seventy-

TABLE 1 (Continued)

CASE No	DURATION OF PENICILLIN TREATMENT		TOTAL DOSAGE OF PENICILLIN units x 10 ³	PRIOR TO PENICILLIN TREATMENT		RESULTS OF CULTURE AT TIME OF GRAFT		AT FIRST CHANGE OF DRESSING	
	BEFORE GRAFT	AFTER GRAFT		Gram Positive	Gram Negative	Gram-Positive	Gram-Negative	Gram-Positive	Gram Negative
	days	days							
1	2	4	600	1		1		1	
2	2	12	1 625	1 4 5	7 12	4	7 8	1 4	7 8
3	4	5	990	1 3 4 5	7	1 5	8	1	7 10
4	1	5	710	1 5		1,5		1 3 5	
5	1	6	750	1	8 9	1 2 3 5	8	1 4 5	8
6	2	4	655	1 5	12	1,3	7 8	1 2 4	7
7	2	5	795	1 5	7 8	1	7 10	Lost	
8	1	9	1 155	1 2	7 8	1 3,5	7 8 11	Lost	
9*	2	6	1 080	1		1 2,6		1 6	8
10	11	9	2 360	1 6	7 9		7†	1	7
11	8	6	1 520	1,5	7	1 3 4	7	1	7
12	42	7	5 880	Lost		1 5	11	Lost	
13	1	9	1 200	1	7 8	4 5	7 8	1	7
13	10	8	2 120	1	7 8	1	7	1 4	7 8
2								1	7 9
3						1 2 3,4 5	7,8	1 2	7 8
7							7 8 9†	1 4	7 8
7								1 4	7 10
10						1 4	7		
11						1 3 4	7	1	8
12								1 4 5	7
13						1	7		
14						3 4,5	7	1 2 5	7,8
15						1 3,4	8	1	7 8
16								1,5	7 8
17						1	9		
18						1,2	7 8 9		
19						1 3,5	7		

KEY TO ORGANISMS: 1 — hemolytic *Staph aureus* 2 — beta hemolytic streptococcus 3 — *Staph albus* 4 — alpha hemolytic streptococcus 5 — diphtheroids 6 — *B subtilis* 7 — *P vulgaris* 8 — *Ps aeruginosa* 9 — *Esch coli* 10 — *K pneumoniae* 11 — *P torquans* 12 — *A faecalis*

and a half to seventy-five years in the penicillin-treated group In Table 3 the results of grafting are given for three age groups, — one to ten years, eleven to fifty years and over fifty years In both the penicillin-treated and nonpenicillin-treated cases all the results in the youngest age group were

five days As shown in Table 4, in the latter group all 7 grafts done in less than median time had takes of 95 to 100 per cent, compared with 4 of the 7

TABLE 4 Results of Grafts with and without Penicillin Treatment according to Time of Grafting and Number of Previous Grafts

NO OF PREVIOUS GRAFTS	TAKE OF GRAFT	LESS THAN MEDIAN TIME		MORE THAN MEDIAN TIME	
		PATIENT TREATED WITH PENICILLIN	PATIENT NOT TREATED WITH PENICILLIN	PATIENT TREATED WITH PENICILLIN	PATIENT NOT TREATED WITH PENICILLIN
	%				
0	95-100	6	4	1	1
	80- 90	0	1	0	0
1	95-100	1	1	0	3
	80- 90	0	0	0	0
2-4	95-100	0	0	3	2
	80- 90	0	1	3	1

TABLE 3 Results of Grafts with and without Penicillin Treatment, according to Age

AGE	TAKE OF GRAFT	PATIENT TREATED WITH PENICILLIN		PATIENT NOT TREATED WITH PENICILLIN	
	%				
5†					
1-10	95-100	5			
	80- 90	0		0	
11-50	95-100	4		4	
	80- 90	2		2	
51 and over	95-100	2		3	
	80-90	1		1	

95 to 100 per cent and thus somewhat better than those in either of the older age groups, in which two thirds of the cases had takes of 95 to 100 per cent

grafts done in greater than median time In the penicillin-treated group, of the 7 grafts done in less than median time 5 had takes of 95 to 100

dressings change after the operation. No penicillin was used locally. In the other 14 grafts, no penicillin or other chemotherapeutic agents were given during this time. Four of the latter patients had

of a small portion of the graft occurred at the edge, but there was no loss of any central area. In the 80 to 90 per cent takes there was some loss of grafted skin in the central areas, as well as losses at the

TABLE 1 Summary of Data concerning 28 Dermatome Skin Grafts in Patients Treated with and without Penicillin

CASE No	AGE	SEX	AREA OF BODY SURFACE BURNED		NO OF PREVIOUS GRAFTS	PERIOD FROM BURN TO GRAFT	AREA OF BODY SURFACE GRAFTED	SITE OF GRAFT	HEMOGLOBIN	PLASMA PROTEIN	TAKE OF GRAFT
			Total	Third degree							
	yr		%	%		days	%		%	gm/100 cc	%
1	2½	M	20	15	1	89	2	Chest	94	7.6	100
2	38	F	40	20	0	51	6	Arm	82	5.4	95
3	58	F	15	10	3	109	5	Arm	94	5.9	90
4	5	F	10	8	0	37	8	Chest and axilla	85	5.7	100
5	32	M	7	2	2	65	2	Arm	102	6.2	85
6	40	M	5	2	0	67	2	Leg	90	6.2	90
7	48	M	20	15	0	63	3	Arm	63	6.6	100
8	45	M	20	12	0	118	2	Legs	84	5.4	95
9*	1½	F	2	2	3*	200	2	Arm	76	6.8	95
10	10	M	15	10	1	116	5	Leg	88	7.5	100
11	6	M	10	5	1	75	3	Leg	87	5.7	95
12	42	F	15	10	0	49	3	Chest and flank	78	6.4	95
13	75	M	20	6	1	111	3	Back	81	6.6	100
13	75	M	20	6	2	120	2	Back	81	5.8	100
2	38	F	40	20	2	80	5	Buttock and thigh	86	5.8	85
3	58	F	15	10	4	126	4	Arm and breast	94	5.8	80
7	48	M	20	15	1	72	6	Arm, back and chest	86	5.7	100
7	48	M	20	15	2	162	3	Chest	85	5.3	95
10	10	M	15	10	0	55	3	Leg	87	5.6	95
11	6	M	10	8	0	44	5	Leg	84	6.6	100
12	42	F	15	10	2	77	4	Buttock and flank	83	7.3	85
13	75	M	20	6	0	24	1	Hands	63	5.1	100
14	16	M	10	5	0	28	2	Thigh	88	6.2	95
15	3	M	6	5	0	35	4	Leg	95	5.8	100
16	45	M	20	15	3	153	3	Arm, chest and axilla	86	5.4	95
17	30	M	1	1	0	44	1	Knee	95	6.4	95
18	57	M	10	3	2	79	3	Leg	88	6.5	95
19	83	F	5	2	0	86	2	Leg	76	5.4	100

*At outside hospital, admitted to Boston City Hospital 180 days after burn.
†Culture was overgrown by *P. vulgaris* and no other organism was recovered.
‡Culture was overgrown by *P. vulgaris* and no gram positive organisms were recovered.

received penicillin earlier for previous skin grafting. At the time of grafting, granulation tissue was cut away when excessive, bleeding being controlled with warm saline packs. If the granulations were not exuberant, the surface exudate was wiped off with dry or saline sponges. All grafts were sewn in place.

RESULTS

The essential data are presented in Table 1. The over-all results of the grafts were approximately the same in both groups, as shown in Table 2. The takes in 11 of the 14 grafts in each group were 95 to 100 per cent, and those in the remaining 6 were 80 to 90 per cent. There was no case of less than eighty per cent take.

There was no essential difference between the 95 and 100 per cent results. In the former a loss

periphery. Some of these areas required small secondary grafts at a later date. For the purposes of discussion in the rest of this paper the 95 to 100

TABLE 2 Results of Grafts with and without Penicillin Treatment

TAKE OF GRAFT	PATIENT TREATED WITH PENICILLIN	PATIENT NOT TREATED WITH PENICILLIN
%		
100	6	5
95	5	6
90	2	0
85	1	2
80	0	1

per cent takes are considered together and are contrasted with those of 80 to 90 per cent.

Sex and Age

There was no significant difference between the patients in the two groups in regard to sex and age.

time of graft or at the first dressing change. Hemolytic *Staphylococcus aureus* was the predominant gram-positive organism, being present in almost every case before and during penicillin treatment.

TABLE 6 Summary of Results of Culture *

ORGANISM	PATIENTS TREATED WITH PENICILLIN			PATIENTS NOT TREATED WITH PENICILLIN		
	TIME OF CULTURE			TIME OF CULTURE		
	Prior to penicillin	At graft	At first change of dressing	At graft	At first change of dressing	
	13 cultures	14 cultures	11 cultures	9 cultures	9 cultures	
Hemolytic						
<i>St. aureus</i>	13*	11	11	8	9	
Beta hemolytic						
streptococcus	1	2	1	2	2	
<i>St. albus</i>	1	4	1	5	0	
Alpha hemolytic						
streptococcus	2	5	4	5	3	
Diphtheroids	6	6	2	1	3	
<i>B. subtilis</i>	1	1	1	0	0	
<i>P. vulgaris</i>	8	8	7	6	8	
<i>Ps. aeruginosa</i>	5	6	4	4	6	
<i>Enter. coli</i>	2	0	0	2	1	
<i>E. pneumoniae</i>	0	1	1	0	1	
<i>P. frag. r11</i>	0	2	0	0	0	
<i>A. faecalis</i>	1	0	0	0	0	

*The figures indicate the number of cultures in which each organism was found.

Beta-hemolytic streptococcus was present in only 1 case prior to the start of penicillin, and after one day of penicillin it disappeared. This organism, however, appeared transiently during penicillin treatment in 3 cases in which the organism had not previously been present. In none of these cases was this organism predominant.

Other gram-positive organisms found were *Staph. albus*, streptococcus with alpha hemolysis, diphtheroids and *Bacillus subtilis*. In no case, however, were these organisms predominant.

Among the gram-negative organisms, *Proteus vulgaris* and *Pseudomonas aeruginosa* were most frequently found, occurring in about half the cases. Other gram-negative organisms (*Escherichia coli*, *Klebsiella pneumoniae*, *Proteus morganii* and *Alkaligenes faecalis*) occurred in only an occasional case. There was no essential change in the number or type of gram-negative organisms under penicillin treatment.

The organisms found in the nonpenicillin-treated cases were essentially the same as in the penicillin-treated group. Hemolytic *Staph. aureus* was the predominant gram-positive organism, being present in almost every case. Beta-hemolytic streptococcus was present in 2 cases at the time of graft and in 1 additional case at the time of the first postoperative dressing. In no case, however, was it predominant. *P. vulgaris* and *Ps. aeruginosa* were the predominant gram-negative organisms.

COMMENT

It appears that the improvement in results of skin grafting of granulating third-degree burns at this hospital that was coincident with the start of this study was not due to penicillin, since the results

were essentially the same in those patients who did not receive penicillin as in those who did. It should be emphasized, however, that the results in the control cases were such that the takes in the penicillin-treated series would have had to be essentially perfect in all cases to show a significant improvement. There was no change in the cultures from, or in the appearance of, the granulating wounds during the period of penicillin treatment. It should be stressed, however, that there were no cases of septicemia or cellulitis, the infection being confined to the local area. In addition, the predominant infecting organisms were hemolytic *Staph. aureus*, *P. vulgaris* and *Ps. aeruginosa*. In no case was beta-hemolytic streptococcus, which has been stated to interfere with the takes of grafts, predominant. It may be, therefore, that under other circumstances, — that is with spreading infection or with other penicillin-sensitive organisms being predominant — penicillin might prove effective.

Some of the factors that may be responsible for the improvement are as follows: first, a better organization for and more experience in the care of burns and the technic of skin grafting, second, a better preparation of the patient by diet, and third, the change in preoperative local preparation that was made to create conditions suitable for a bacteriologic study — that is, the substitution of infrequently changed dry dressings for frequently changed wet dressings. Hirschfeld⁵ states that he also changed his preoperative technic in a similar fashion for all but 2 of the patients in his penicillin-treated series.

Because of the absence of a control series of cases done with preoperative frequently changed wet dressings during the same period of time as the dry-dressing cases, it cannot be stated with certainty that the change in preoperative treatment was the essential factor in the improvement of the results. On the other hand, the results in the present series show that frequent time-consuming and painful wet dressings are not necessary, and that the simplest of pressure dressings (dry sterile), infrequently changed, is a good form of preparation for dermatome skin grafts.

SUMMARY

Twenty-eight dermatome skin grafts have been studied.

Half the cases received parenteral penicillin treatment before and after grafting, and the other half received no penicillin.

In other respects the technics used in the two groups were identical. Dressings before and after grafting were dry sterile pressure dressings with adequate splinting. The condition of the patients, the extent and site of the burns and the extent of the grafts were similar in the two groups.

All granulating areas were locally infected, but there were no cases of spreading infection.

per cent, compared with 6 of the 7 done in greater than median time. In each group the two grafts done at the longest times after the burn had takes of 95 to 100 per cent.

Previous Grafts

In Table 4 the cases are arranged according to the number of previous grafts. About half the cases in each class had had no previous grafts, and the remainder had had from one to four previous grafts. It appears that the results in both groups were better in those patients who had had no previous graft or only one, since of the 18 such grafts 17 had takes of 95 to 100 per cent, compared with 5 of the 10 grafts in patients who had had 2 or more previous grafts.

Site of Graft

There were no significant differences between the areas grafted in the two groups. Seventeen grafts were done on the extremities alone, 4 on the extremities together with some other areas, and 7 elsewhere. No significant differences in results were associated with the area grafted.

Severity of Burns

In Table 5 the cases are arranged according to the percentage of body surface involved in third-degree burns and the percentage of body surface

TABLE 5 Results of Grafts with and without Penicillin Treatment according to Percentage of Body Surface Burned (Third-Degree) and of Body Surface Grafted

AREA OF BODY SURFACE GRAFTED	TAKE OF GRAFT	PERCENTAGE OF BODY SURFACES BURNED			
		2-10%		15-20%	
%	%	Patient Treated with Penicillin	Patient not Treated with Penicillin	Patient Treated with Penicillin	Patient not Treated with Penicillin
1-2	95-100	4	3	0	1
	80-90	0	1	0	0
	95-100	4	5	3	3
3-8	80-90	2	1	1	0

grafted. There were no significant differences between the two groups regarding results or distribution of cases, 10 of the 14 grafts in each group having 10 per cent or less third-degree burns and two thirds of the patients in each group having 3 to 8 per cent body surface grafted at the operation under study.

Hemoglobin

No conclusions can be drawn concerning the possible effect of anemia on the results of the grafts, since most of the patients in each class had a hemoglobin of over 75 per cent at the time of grafting. There was 1 patient in each class with a hemoglobin of 63 per cent at the time of grafting. Neither of these patients received transfusions in the immediate postoperative period. In each of these cases the take was 100 per cent. It is recommended,

however, that no grafts be done on patients with less than 80 per cent hemoglobin.

Plasma Protein

The cases have also been analyzed in respect to plasma protein concentration at the time of grafting. In this laboratory concentrations of over 5.5 gm per 100 cc are considered normal, those below 5.0 gm are considered definitely low, and those between 5.0 and 5.5 gm are graded as borderline. No definite conclusions can be drawn concerning the effect of hypoproteinemia, since none of the patients had definitely low plasma proteins. Most patients in each group had definitely normal plasma protein concentrations, but in 6 grafts—2 in the penicillin-treated group and 4 in the nonpenicillin-treated group—the patients had a plasma protein between 5.0 and 5.5 gm. None of these patients, however, had peripheral edema. The takes in all these 6 cases were 95 to 100 per cent.

Fever

Cases not receiving penicillin. In 5 grafts in the nonpenicillin-treated group, the patients had low-grade fevers during the week preceding grafting, the average temperature being 100.1°F, with extremes of 99.4 to 101.5°F. In 4 of these, the patients continued to run a low-grade fever after grafting, and in 1, the patient became afebrile. In 2 of these, including the patients who became afebrile, the takes were 80 to 90 per cent. In only 1 of the 9 grafts in patients who were afebrile in the week preceding grafting was there a take of less than 95 to 100 per cent. This patient had become febrile postoperatively and had a take of 80 per cent.

Cases receiving penicillin. In 9 of the grafts in the penicillin-treated group the patients had low-grade fevers during the week preceding the start of penicillin, the average temperature being 99.8°F, with extremes of 99 to 101°F. Only 1 of these became afebrile. In 4 there was some drop in temperature, and in the remaining 4 there was a slight rise. The average temperature of the febrile group descended from 99.8 to 99.3°F. Three became afebrile during the postoperative period. There was no apparent influence of the presence of fever on the results, since of the 6 grafts in patients who were afebrile both before and after grafting 5 had takes of 95 to 100 per cent, compared with 4 of the 5 in patients who were febrile before and after grafting.

Bacteriology

There were no cases of spreading infection, but all the granulating wounds were locally infected. The results of cultures taken from the granulating areas are detailed in Table 1 and summarized in Table 6. In the penicillin-treated group there were no significant differences between the cultures or the amount of exudate prior to penicillin, at the

angles of the mouth, inspecting the gums to detect swelling, bleeding, sponginess or abnormal color, inspecting the teeth for premature extractions, cavities and fillings, feeling the chest for abnormalities of the breastbone or ribs, in many cases the upper clothing being removed and the chest in-

an effort to gain the approval of the person taking the history. Again, evaluation of the diets on a quantitative basis is impossible, for no standard of food measurement can be established except by servings. It is believed, however, that with a large group of children such surveys may be used to in-

TABLE 1 Summary of Number of Examinations

GROUP	AGE RANGE	BOYS	GIRLS	NO OF SUBJECTS	HEIGHT AND WEIGHT	DIETARY HISTORY	PHYSICAL EXAMINATION	ASCORBIC ACID LEVEL	HEMOGLOBIN LEVEL	X-RAY EXAMINATION
A	6-9	17	10	27	27	27	26	25	25	2
B	8-13	14	46	60	14	68	60	62	63	0
C	10-13	15	14	29	2	24	29	15	17	0
D	12-15	15	11	26	26	26	25	26	26	0
E	5-12	10	10	20	0	0	18	20	20	0
F	8-14	13	5	18	18	18	17	11	2	0
G	8-14	13	10	23	23	23	23	17	17	0
H	5-14	83	70	153	0	0	153	0	0	8
Totals		210	176	386	170	186	381	176	170	10

spected, examining the skin of the back of the upper arm for evidence of abnormal follicles with the side of the thigh also frequently examined, and inspecting the knees and legs for evidence of knock-knees or bowlegs. When possible, the height and weight were recorded. Unless positive signs were found, the child was not questioned regarding any symp-

dicant trends, individual differences tending to balance one another.

In Table 2 is shown the number of diets that contained potatoes, other vegetables, fruits, citrus fruits or tomatoes, milk, and meat and eggs. The diets were evaluated with regard to their apparent adequacy, as follows: Good, one or more servings

TABLE 2 Diet Summary

GROUP	NO OF SUBJECTS	POTATOES	OTHER VEGETABLES	FRUITS	CITRUS FRUITS OR TOMATOES	MILK	MEAT AND EGGS
Urban groups							
A	27	24	19	10	21	27	24
B	68	57	57	45	45	61	64
C	24	20	9	12	4	19	34
D	26	24	20	17	12	25	34
Totals	145	124 (85%)	85 (59%)	84 (58%)	82 (57%)	152 (91%)	176 (94%)
Rural groups							
E	18	14	9	10	15	18	12
G	23	21	8	15	15	25	19
Totals	41	35 (85%)	17 (41%)	25 (56%)	0 (74%)	41 (100%)	31 (76%)
Urban and rural groups	186	159 (85%)	102 (55%)	107 (58%)	112 (62%)	173 (93%)	167 (90%)

toms he had experienced, and the procedure was based only on what could be seen or felt.

X-ray Examination

X-ray films of the knees and wrists of 10 children were taken.

RESULTS

A summary of the examinations is presented in Table 1, together with the age range and the number of boys and girls in each group.

Diet Survey

We recognize the inadequacy of a one-day record of food intake, for this method does not give a satisfactory picture of food habits. The child's memory may be poor, or he may make false statements in

from each food group of the basic seven, with at least two servings of vegetables other than potato or five servings of all fruits and vegetables and two servings of milk. Fair, at least four servings of all fruits and vegetables and one serving from each other group. Poor, fewer than four servings of fruit and vegetables, with one or more other groups missing. Of the 186 one-day diet histories, 24 per cent were rated as good, 23 per cent as fair and 51 per cent as poor.

Ascorbic Acid Levels

The ranges of plasma ascorbic acid levels according to groups are shown in Table 3. The data in Table 4 show the numbers and percentages of children having plasma ascorbic acid levels of 0.6 mg per 100 cc or less and the percentages of those who had citrus fruit or tomatoes on the day of the test.

Hemolytic *Staphylococcus aureus*, *Proteus vulgaris* and *Pseudomonas aeruginosa* were the predominant organisms

Penicillin had no effect on the bacterial flora or the appearance of the wounds

The results in both groups were excellent

Simple dry sterile pressure dressings, infrequently changed, are recommended before and after skin grafting

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NUTRITIONAL DEFECTS AMONG CHILDREN IN VERMONT*

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DIET surveys, such as those reported by the National Research Council,¹ have revealed that many New Englanders are not eating adequate quantities of protective foods. This condition is reflected by the high incidence of selective service rejections in the area. The object of this study was to determine the nutritional status of a group of Vermont children in the vicinity of Burlington.

EXPERIMENTAL METHOD

Selection of Children

Children were selected so as to include urban and rural areas, different ages, different economic status and two institutions for child care. A total of 386 were inspected for physical signs, and blood analyses for vitamin C and hemoglobin were completed on 176 and 170, respectively. In the city, children in six classrooms were studied in addition to those in the institutions. The children were classified as follows: Group A, high-income area, Groups B and D, both low-income and high-income areas, Group C, low-income area, Groups F and G, rural areas, and Groups E and H, children's homes. The age range in rural schools and at each of the two institutions was greater than that in the separate grades at the city schools.

Diet Survey

Sheets were prepared for recording food consumption at breakfast, midmorning, lunch, midafternoon

*This study was made during September and October 1944 under the auspices of the Vermont State Nutrition Committee.

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and dinner and in the evening. Records of food intake for one day were then obtained from children in the school groups under the supervision of teachers and nutritionists.

Ascorbic Acid Levels

Oxalated venous blood from nonfasting subjects was used for the determination of ascorbic acid. Nearly all the samples were obtained between 10 and 11 a m., except for a group of 26 children whose blood was taken between 2 and 3 p m. All samples were taken to the laboratory within ninety minutes, and ascorbic acid was determined in the plasma according to the method of Mindlin and Butler,² using the Klett-Summerson photoelectric colorimeter.

Hemoglobin Levels

The acid hematin method was used as outlined in the directions issued with the Klett-Summerson photoelectric colorimeter. The reference point, however, was established by reading several of the acid hematin solutions with the optical colorimeter, using a hemoglobin attachment.

Physical Examination

The inspection of school children was not in any sense a complete physical examination, rather it was a careful search for a few specific signs related to the past or present nutritional status of the child. The inspection included feeling the head for evidence of parietal bossing, inspecting the eyelids for evidence of inflammation or crusting, inspecting the outer angle of the eyes for cracks, scars or sores, pulling down the lower eyelid for a better view of the lid margin and lining, inspecting the lips for evidence of cracks, sores or scars at the

In low-income urban areas, breakfasts were notably poor, few including citrus fruits, tomatoes or cereal. Unfortunately, toast or buns or doughnuts and coffee were often the only foods used for this important meal. The other meals were usually adequate with regard to calories but were low in their content of protective foods.

Protein intake, as judged by the use of meat and eggs, appeared to be satisfactory. Nearly all the children received milk, but smaller amounts were used in low-income than in high-income groups. It is evident that many parents have little knowledge of the meaning of an adequate, not to mention an optimal, diet. This again emphasizes the need of nutrition education within the home.

In rural areas, the intake of fruits and vegetables was low, although tomatoes were widely used. Every child was drinking some milk, but often in inadequate amounts. The protein intake of the rural children was less than that of urban children.

The infrequent appearance of eggs on all diet records was conspicuous. Records of urban junior-high-school children revealed a high consumption of sweets and soft drinks.

The children in Group E, although living in the city, had diets more similar to those of the rural groups than to those of the other urban groups. Protein intake, as reflected by use of meat and eggs, was on the low side of normal, but in contrast to rural groups, fruits and vegetables were more frequently used.

Ascorbic Acid Levels

Although deficiency of ascorbic acid is not infrequent,^{1, 4, 5} the fact that so many low blood values were found at this time of year — namely, at the end of summer when tomatoes were plentiful — is surprising. Rural children in general had levels higher than those of urban children, undoubtedly owing to the generous use of tomatoes. In the city, children from low-income areas tended to have subnormal amounts of ascorbic acid, from the standpoint both of diet and of blood findings (Tables 2, 3 and 4). Admittedly citrus fruits and tomatoes had been costly during the summer, yet unrationed citrus juices were freely available at moderate cost. In general the blood findings corresponded with dietary reports of the use of tomatoes and citrus fruits, and there was a close group correlation between physical findings as shown by the condition of the gums and the ascorbic acid levels of the blood. Physical examination revealed that approximately 40 per cent of the entire series had a mild gingivitis. In the group having blood determinations, 25 per cent had values below 0.6 mg per 100 cc.

Examination of the gums did not show the serious conditions that are seen with frank scurvy, nearly all of the positive findings being classed as mild. It is known that the summer diet in this area includes

more ascorbic acid than does the winter diet, so that one might expect quite a different set of findings at the end of the winter season.

Hemoglobin Levels

From the data on hemoglobin values, it appears that approximately 6 per cent of the children had levels indicative of a mild anemia. Comparing the percentages shown in Table 5, it is seen that rural children had lower average values than did urban children. Again, economic status is reflected by urban groups, percentages of low hemoglobin values being higher among children from low-income areas. As mentioned earlier, protein intake in rural and low-income groups was somewhat less than that in high-income groups, and this may serve as one explanation of the lower values.

Physical Findings

Eyes For some years it has been known that vitamin A has an important role in the nutrition of the eye, and more recently Sydenstricker et al⁶ have demonstrated the need of riboflavin. Certain signs seem to arise from a lack of either of these two vitamins, whereas others seem more or less specific for the individual vitamin.

Crusting of the eyelids was noted among 14 per cent of the children. No acute sores were noted at the outer angles of the eyes, yet a few children showed scarring at these points. Of the children who showed some positive signs in connection with the eyes, a number reported stinging, burning or itching, photophobia or similar symptoms. Visual acuity was not tested, since it had been carried out as part of the regular school examination.

There was a high prevalence of granulated lids or follicular conjunctivitis in certain groups of children. This condition has been associated with vitamin A deficiency, since it is sometimes relieved by a large amount of this vitamin.

Mouth The incidence of spongy, bleeding gums was low, and nearly all cases recorded as positive showed questionable or mild states. Since this condition is often associated with ascorbic acid deficiency, it is not surprising that few severe cases were noted at the time of examination (early October), for it is likely that the summer diet in this area contains considerably more ascorbic acid than does the winter diet. Similar to the observations of Crane and Woods,⁶ our examinations revealed but few of the markedly swollen, spongy or bleeding gums typical of frank scurvy.

Cracks, sores or scars at the corners of the mouth may, of course, be due to a variety of causes. They may be associated with riboflavin or pyridoxine deficiency.^{7, 8} Further study, including therapeutic tests, would be necessary to confirm the theory that conditions such as those found in this series of children represent a riboflavin deficiency. This condition was not prevalent among the children ex-

There is some question concerning what plasma level should be considered as the lower limit for adequacy^{1, 2} Abt and Farmer³ have stated, "Blood

TABLE 3 Range of Plasma Ascorbic Acid Levels

GROUP	PLASMA ASCORBIC ACID LEVEL (MG PER 100 CC)				
	0-0.19	0.20-0.39	0.40-0.59	0.60-0.99	1.00-1.99
Urban groups					
A	1	2	1	9	12
B	2	6	9	31	14
C	7	3	2	6	2
D	0	3	1	7	8
E	0	1	0	2	17
Totals	12 (8%)	15 (10%)	13 (9%)	55 (37%)	53 (36%)
Rural groups					
F	0	0	0	0	11
G	0	1	1	4	11
Totals	0	1 (4%)	1 (4%)	4 (14%)	22 (78%)
Urban and rural groups	12 (7%)	16 (9%)	14 (8%)	59 (34%)	75 (42%)

plasma values below 0.7 mg per 100 cc are subnormal or at least suboptimal" On their chart, the beginning scurvy level is shown as lying between

TABLE 4 Data on Number and Percentage of Low Plasma Ascorbic Acid Levels and Percentage of Children Who Had Had Citrus Fruit or Tomatoes on Day of Test

GROUP	LEVEL BELOW 0.6 MG PER 100 CC.		CITRUS FRUIT OR TOMATO ON DAY OF TEST
	NO	PERCENTAGE	
Urban groups			%
A	4	16	64
B	17	27	39
C	9	60	7
D	11	42	38
E	1	5	100
Total	42	28	48
Averages			
Rural groups			
F	0	0	83
G	2	12	65
Total	2	7	71
Averages			
Urban and rural groups	44	25	52

0.5 and 0.6 mg We have therefore considered concentrations of 0.6 mg or less as subnormal

Hemoglobin Levels

As is the case with vitamin C, various standards have been used in interpreting hemoglobin data

TABLE 6 Summary of Physical Findings in All Groups

	NOT PRESENT		MILD		MODERATE		MARKED		SEVERE	
	NO	PER CENTAGE	NO	PER CENTAGE	NO	PER CENTAGE	NO	PER CENTAGE	NO	PER CENTAGE
Crusted eyelids	328	86	44	12	9	2	0	0	0	0
Scars at corners of eyes	368	97	6	2	7	2	0	0	0	0
Angular stomatitis	330	87	30	8	11	3	10	3	0	0
Scars at corners of mouth	320	84	40	11	16	4	5	1	0	0
Gingivitis	215	62	81	21	56	15	8	2	1	0.3
Active or healed rickets	119	33	126	36	87	24	21	6	1	0.3
Head	145	38	151	40	75	20	9	2	1	0.3
Chest	327	86	42	11	10	3	2	0.5	0	0
Knees	231	61	50	23	52	14	4	1	4	1
Folliculosis										

Levels below 13.5 gm per 100 cc are assumed to indicate a dietary inadequacy of iron¹ Results of the hemoglobin study are presented in Table 5

Physical Findings

A summary of the findings regarding the specific conditions looked for is given in Table 6 An attempt has been made to determine the prevalence and severity of these conditions Admittedly, the degree of severity is not a quantitative criterion, but rather a crude estimate of the degree of abnormality taken as a whole

DISCUSSION

Heights and Weights

No valid method for detecting poor nutrition by means of any of the usual indices of body build has been discovered It is generally agreed, however,

TABLE 5 Data on Hemoglobin Levels

GROUP	HEMOGLOBIN LEVEL (GM PER 100 CC)			
	11.0-13.4	13.5-14.9	15.0-16.4	16.5-17.9
Urban groups				
A	0	2	21	2
B	0	13	41	9
C	2	8	5	2
D	0	7	15	4
E	7	8	5	0
Totals	9 (6%)	38 (25%)	87 (58%)	17 (11%)
Rural groups				
F	0	0	2	0
G	1	12	4	0
Totals	1 (5%)	12 (63%)	6 (32%)	0
Urban and rural groups	10 (6%)	50 (29%)	93 (55%)	17 (10%)

that all normal children show growth when measured over a period of several months Measurements will again be made in the spring of 1946 to determine the rate at which these children are growing

The heights and weights were obtained from school records of physical examinations made in the previous fall Weights were compared with the average for height and age according to the Baldwin-Wood tables Only the children 10 per cent over or under the average weight were considered as showing a significant deviation from normal Data for 130 children were available Of this number, 18 (14 per cent) were found to be more than 10 per cent under average weight, and 23 (18 per cent) more than 10 per cent over average weight

Diet Survey

Without doubt economic status plays an important role in the nutritional well-being of children

manent in nature. These findings, however, if interpreted as indicating previous rickets, should be of value regarding infants and younger children residing in this area. No attempt was made to learn which of the children had received antirachitic substances or in what amounts. It can be assumed that if such substances were used, inadequate quantities were given. Moore et al⁹ state that 80 per cent of the children they examined were reported to have had an antirachitic substance of one kind or another.

X-ray plates of the wrists and knees of several selected children indicated chronic rickets, with sporadic deposition of lime salt. This may have been due to interrupted dosage with antirachitic substances, to climatic changes or possibly to other factors.

In studying the utilization of calcium and phosphorus by preschool children, Pierce et al¹⁰ found that satisfactory retention ratios were not obtained until the dosage of antirachitic substance amounted to 1800 international units of vitamin D daily. These observations lead one to question whether the national standards of dosage are adequate for present-day infants and children in this section of the United States. Included in this series of children are those born during the so-called "depression years," a fact that again involves the problem of economic status.

SUMMARY

A survey of the nutritive status of 386 Vermont school children, selected so as to represent rural and urban groups of various ages and economic levels, has been made.

A review of the food intake showed the greatest fault to lie in the low intake of fruits and vegetables.

Blood studies revealed that 25 per cent of a group of 176 children had plasma vitamin C levels below 0.6 mg per 100 cc, and on physical inspection 40 per cent of the entire series had inflammation of the gums of varying intensity. Severe forms of spongy, bleeding gums were found in only a small percentage of the children.

Six per cent of 170 children had low hemoglobin values suggestive of a mild anemia. Urban children had higher hemoglobin levels than did rural children.

Skeletal changes usually associated with rickets were found in about 85 per cent of the children. The signs chosen were looked for with extreme care, and even minor deviations were included.

Signs associated with a shortage of riboflavin were also found in a small percentage of the children, but they cannot be accepted as definitely indicating any serious deficiency of this vitamin.

Some degree of folliculosis, at least of the outer aspect of the arm, was found in 40 per cent of the children, and 5 of these subjects had a generalized folliculosis of a marked degree. Mild cases of follicular conjunctivitis were frequent.

Premature loss of the teeth and dental caries were found to be extremely prevalent, even on gross examination with a good light and a tongue depressor.

We are indebted for their co-operation to the College of Medicine, University of Vermont, the Vermont State Department of Public Health, the United States Public Health Service, the Vermont Agricultural Extension Service, the Vermont Catholic Charities and the officials of public and parochial schools as well as those of the Children's Home and Saint Joseph's Orphan Asylum.

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amined, but this should not be taken as indicating that their riboflavin intake was necessarily adequate.

Smoothness of the tongue was not recorded but was observed in a small number of children while the mouth was being inspected. This was also true in regard to purplish discoloration of the tongue. No case of beefy redness of the tongue was noted.

Pale mucous membranes suggesting anemia were not recorded, but this condition was observed in extremely few children.

Teeth Although a great deal of experimental work has been done on the relation between dental caries and nutrition, we are still very much in the dark on this subject. Since mouths were being inspected, it was thought worth while to record gross findings concerning premature loss of teeth and dental caries. This should not be regarded as a dental examination of the type executed by a dentist, rather, it included an inspection for missing teeth and gross cavities or fillings that could be seen in a good light with a tongue depressor. A more thorough examination would undoubtedly have revealed additional small cavities.

Dental defects of the type looked for were extremely frequent. Children in one grade at the junior high school had an average of 5.2 decayed, missing or filled teeth, a regrettable finding in view of the fact that these were relatively new, permanent teeth. There are undoubtedly several reasons for the marked prevalence of dental caries in this area. In sections of the United States in which a small amount of fluorine is present in the drinking water, the incidence of dental caries is less than in regions where the water does not contain fluorine. Data collected by the Vermont State Board of Health reveal that nearly all the waters studied have been free of fluorine. We are not yet in a position to say definitely that fluorine is a nutrient required by teeth, but present indications are that about one part per million of fluorine in the drinking water greatly decreases dental caries among young children. There are also indications that fluorine therapy is most effective up to eight years of age.

In view of the widespread use of milk by these children, it does not seem likely that there is any serious deficiency of calcium and phosphorus, but there may be a defect in utilization. This is discussed in more detail under the section dealing with bones.

Skin There is much interest in skin manifestations of vitamin A deficiency. One condition of the skin — namely, folliculosis — was looked for. The lesions may be localized or more or less widespread over the body. For convenience and speed, the posterolateral aspect of the upper arm was chosen for inspection. Since this condition may occur on other parts of the body without occurring on the arm, some cases may have been missed. This is not highly important, for the finding of a few addi-

tional cases would not have appreciably changed the picture. When the finding was recorded as "not present" either no lesions on the arm were observed or an occasional abnormal follicle was seen. The cases recorded as mild showed a few definite lesions, and such children were usually not further examined. Those recorded as moderate showed somewhat larger and more numerous follicles on the sides of the arm, and those listed as marked revealed this condition to a greater extent than did the preceding group. Only 5 cases were designated as being severe, and in them the folliculosis was noted over a considerable part of the body. Two of these children were a brother and sister whose mother also had a severe form of the condition. Two others were sisters, and the fifth reported that her older sister had the condition to a marked extent. The results show that the milder forms of folliculosis were frequent, and in nearly all cases it had not been noticed by the child, no inquiry was made whether other members of these families had a similar condition.

Granulated eyelids or follicular conjunctivitis was frequently noted. This may be said to be a condition of the eyelids that resembles folliculosis of the skin.

For some years folliculosis has been associated with lack of vitamin A, but other factors may be involved. For example, the brother of the girl who had a severe condition had been out-of-doors much of the summer, with the upper part of his body exposed to sunlight, and the skin manifestations were not so serious on the upper body as those noted in the girl, who had not been similarly exposed. Furthermore, folliculosis on the face was rarely seen. This leads one to speculate on the role of sunlight and vitamin D. Again, the amounts and kinds of food eaten, as well as other possible variables, must be considered.

Bones If the signs recorded indicate a history of rickets, it can be said that mild rickets was extremely frequent in this series. Although these signs were carefully looked for, they were necessarily rather crudely classified with regard to severity. It should be mentioned that moderate parietal bossing was found in many small children who showed no apparent abnormality of the chest or knees. Also, findings on the chest or knees were not always accompanied by parietal bossing. If one considers the series collectively, it is seen that approximately 85 per cent of the children had one or more abnormalities usually accepted as indicative of rickets. Moore et al.⁹ report a similar high incidence of rickets among children in two meteorologically different localities on the Pacific Coast.

Assuming that nearly all the signs of rickets were residual and did not represent active rickets, the findings are relatively unimportant so far as the children examined are concerned, because the bone changes had occurred and were more or less per-

joints or abnormal x-ray films or laboratory findings, the fatigability, anorexia, weight loss and vague or inconstant pains in joints or muscles are ascribed to psychogenic factors. Since there is no specific diagnostic test, it is often impossible to make the correct diagnosis until characteristic joint signs and abnormal roentgenographic findings appear.

CASE 7 A 21-year-old unmarried stenographer was admitted to the hospital on June 30, 1932, because of recurrent attacks of pain in the region of the right buttock and posterior aspect of the right thigh for the preceding 7 months. In November, 1931, while taking gymnastics, she had for the first time experienced pain in the right hip. Within a few months this pain was provoked by ordinary activity. The resultant disability obliged her to stop working. Her physician stated that she had sciatic rheumatism and advised her to rest. Within the next few months she consulted three other physicians and received manipulations and subsequently strapping of the back, to no avail. X-ray examination of the lumbar spine and pelvis was negative.

Ten days after admission, the patient was discharged with a diagnosis of psychoneurosis. No abnormalities had been discovered by physical and neurologic examinations. The blood-cell count and urine examination were not remarkable. A blood Hinton reaction was negative. Chemical and serologic analysis of the spinal fluid was negative.

After discharge from the hospital the patient was treated with psychotherapy for several months. There was thought to be some improvement, and in the fall of 1932 she returned to work. It was not until December 9, 1935, that she was again seen. During her 3 years' absence she had had almost constant discomfort from pain in the back and right hip punctuated at intervals by severe exacerbations. Deep breathing and coughing had caused pain in the chest.

At the time of this admission, examination showed a thin girl who stooped forward when standing. The lumbar spine was immobile. There was restricted mobility of the thoracic spine and practically no chest expansion. The neck could be flexed only 10°, and it could not be rotated beyond 35° bilaterally. X-ray examination of the spine was negative except for increased density of the bone about the sacroiliac joints and irregularity of these joints. The corrected sedimentation rate was 103 mm per minute. A diagnosis of rheumatoid spondylitis was made.

During the hospital stay most of the pain disappeared and the position of the back improved. The chest expansion increased to 4 cm. Following discharge on January 25, 1936, occasional exacerbations of pain in her back and left hip continued for 5 years. During this interval the patient gained weight, but the sedimentation rate remained rapid. Symptoms gradually subsided and she returned to work. In March, 1943, she was working 6 days a week without symptoms.

The difficulty of making a definite diagnosis in the early stage of rheumatoid arthritis is demonstrated by this case. Characteristically, patients consult many physicians during this period because of the severity of the symptoms. Many diagnoses are made, and the symptoms fail to respond to the relatively inadequate types of therapy that are suggested. Often such patients are finally considered to be psychoneurotic. In the above case the disease was only moderately severe, as indicated by the subsequent course, and presumably would have become quiescent without much joint damage if a proper regime had been instituted early in the illness.

The palindromic syndrome described by Hench¹³ is manifested by multiple, usually afebrile, attacks of acute pain, swelling, redness and tenderness in the region of one or more joints. The attacks ap-

pear suddenly, last only a few hours or days and leave no residual signs. Often firm, red, tender swellings on the malleoli, heels or finger pads or near joints and occasionally intracutaneous nodules appear with the attacks and last for a few days to weeks. The sedimentation rate is occasionally slightly elevated. In Hench's experience, this syndrome occurred in patients who did not have rheumatoid arthritis. The majority of the cases of palindromic syndrome seen in this clinic have occurred in patients with definite evidence of rheumatoid arthritis—such evidence as fusion of sacroiliac joints or other characteristic x-ray changes or progressive, symmetrical joint disease. In several cases the syndrome of multiple, recurrent attacks of pain, swelling and redness has been the manifestation of the initial stage of rheumatoid arthritis, as in the following case.

CASE 8 A 19-year-old student was admitted to the clinic on February 7, 1936, because of intermittent attacks of pain and swelling of various joints during the preceding 3 months. In November, 1935, while she was apparently in good health, the proximal interphalangeal joints of the hands suddenly became painful, stiff and swollen. Over a period of 2 weeks one midphalangeal joint after another was affected, each joint being involved for 2 days. Following this episode, she was perfectly well for 1 month. At that time similar symptoms recurred, involving the right wrist and left elbow as well as the midphalangeal joints of the fingers. Once again the symptoms disappeared within 2 weeks only to return 2 weeks later. Thereafter the attacks recurred until the time of admission, being manifested in the fingers, wrists, right elbow, both ankles and the metatarsophalangeal joints on the right. The past history was noncontributory. The paternal grandmother had had "arthritis" and the mother had had "inflammatory rheumatism" in childhood.

On examination at admission the heart was normal except for a Grade 2 systolic murmur at the apex and along the left of the sternum. The only abnormalities in the joints were slight pain, tenderness and swelling of the midphalangeal joints of the right 5th and left 2nd fingers. The corrected sedimentation rate was 0.86 mm per minute. Urine examination was negative. The electrocardiogram showed no abnormalities. X-ray films of the hands were normal except for slight soft-tissue swelling around the midphalangeal joints.

On a regime of increased rest, aspirin as necessary and added vitamin A and vitamin B complex the attacks of joint pain and swelling became less frequent, and in July, 1936, they disappeared, although slight discomfort in both wrists continued. Examination of the joints at that time showed slight swelling over the radial side of both wrists, extending up the arms for several centimeters. In these regions there were also small nodules, apparently in the tendon sheaths. The sedimentation rate had fallen to 0.39 mm per minute.

During the following year the patient was absolutely symptom free and gained weight. In July, 1937, she had a paratyphoid infection, and 2 weeks later noted recurrence of attacks of joint pain and swelling involving various joints and persisting for 1 or 2 days. The skin over the affected joints was usually slightly reddened. She lost 12 pounds in weight and had moderate fatigability. On resumption of daily rest periods and aspirin the attacks became less frequent, but they continued to recur at intervals varying from 1 week to 3 months. Occasionally subcutaneous and intracutaneous nodules appeared on the palmar surfaces of the fingers.

From 1940 to 1943 the attacks were relatively infrequent. In 1944, however, marked fatigability recurred and the attacks became more frequent, until finally, early in 1945, there were symptoms in some joint almost every day. The increase in symptoms occurred at a time when the patient was working hard and carrying great responsibility.

Examination in April, 1945, showed subcutaneous nodules below the olecranon on both sides and large nodules over the Achilles tendons. There was persistence of thickening above

MEDICAL PROGRESS

RHEUMATOID ARTHRITIS. ITS VARIED CLINICAL MANIFESTATIONS (Concluded)*

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Another traumatic condition that is often simulated by rheumatoid arthritis is ruptured intervertebral disk.¹¹ Persistent low-back pain, increased by coughing or sneezing, radiation of pain down the legs, often over nerve-root distributions, and areas of hyperesthesia or hypesthesia on the legs are frequent manifestations of rheumatoid spondylitis. In such patients one can often obtain a history of trauma preceding the onset of symptoms. Such trauma, which may have been coincidental or may have been a precipitating factor in the rheumatoid arthritis, is usually assumed to support the diagnosis of ruptured disk. An elevation of the spinal-fluid protein is often found in rheumatoid spondylitis¹² and does not aid in the differential diagnosis. As in the case of the differentiation of rheumatoid and traumatic arthritis, evidence of involvement of other joints, constitutional symptoms, roentgenologic evidence of narrowing and irregularity of the sacroiliac joints or elevation of the sedimentation rate indicates the presence of rheumatoid arthritis. One of the chief problems in such cases is to determine whether the symptoms are entirely due to the rheumatoid arthritis or arise in part from a coexistent ruptured disk. In some cases that present signs and symptoms suggesting a ruptured disk, the diagnosis of rheumatoid arthritis is not made until after operation, as in the following case. Such an occurrence is unfortunate, since the operation itself may cause an exacerbation of the arthritis.

CASE 6 A 28-year-old, married truck driver was admitted to the hospital on December 26, 1944, because of pain in the back and left leg of 4 months' duration. In March, 1944, he developed a dull pain in the lumbar region, following a twisting injury to the back. This persisted unchanged for 3 months, at the end of which time he began to experience repeated episodes of sudden, severe pain in the lumbar region, which radiated to the left gluteal region, thigh, calf of the leg, lateral aspect of the foot and 4th and 5th toes. There was occasional radiation to the pubic region. The pain was accompanied by numbness over the lateral aspect of the left foot. It was occasionally precipitated by forward bending, coughing, deep breathing or sudden jarring, but also appeared without apparent precipitating factors. It was increased by coughing and sneezing. The pain became so severe in October that the patient stopped working.

The past history revealed an episode of furuncles for several months preceding the onset of the present illness. No

history of previous joint involvement was elicited at that time. Two brothers had complained of back pain, the etiology of which was not known.

Examination on admission revealed a slight limp. There was marked splinting of the lumbar spine, with limitation of motion. Straight leg-raising was possible to 30° on the left and 85° on the right. There was local tenderness over the 5th lumbar vertebra and hypesthesia over the anterior aspect of the left thigh and the lateral aspect of the left ankle. The reflexes were normal. X-ray examination of the lumbar spine revealed disk spaces of normal width. There was slight narrowing of the anterior portion of the body of the 1st lumbar vertebra. A slight amount of new bone formation was seen about the right sacroiliac joint. Lipiodol myelography showed no abnormality of the spinal canal. Routine urine and blood examinations were negative. The spinal-fluid protein was 40 mg per 100 cc. The sedimentation rate was not determined.

A diagnosis of ruptured intervertebral disk was made, and a lumbar laminectomy was performed on January 5, 1945. There appeared to be anterior bulging of the disk between the fifth lumbar and first sacral vertebrae. No free fragment could be found. The posterior longitudinal ligament, which was intact, was incised and the disk was removed in numerous small bites. The pain in the leg began to improve on the 2nd postoperative day, but the pain in the back persisted. The patient was discharged with a back brace on January 20.

Following discharge, the pain became progressively severer. In addition to the areas involved preoperatively, the patient developed pain radiating to the groins and testicles. He was readmitted on February 17, 1945. With more intensive interrogation, it was found that he had had joint symptoms preceding the onset of the back pain. The shoulders had been painful in 1933, with frequent recurrence during the following 10 years. In 1942 the hands were painful, and soon thereafter there was excessive fatigability, aching in the muscles of the legs and pain in his temporomandibular joints, right sternoclavicular joint and both feet. Because of these symptoms the patient left his work in a mill to seek a less strenuous occupation.

Examination on readmission showed persistence of splinting of the lumbar spine, with moderate paravertebral tenderness in this region. X-ray films of the lumbar spine revealed no definite change. The corrected sedimentation rate was 0.52 mm per minute. A diagnosis of rheumatoid arthritis was made.

On a regimen of complete bed rest, aspirin, hot packs to the back and generalized exercises the pain improved markedly, and the patient was discharged on April 21, free of all symptoms except slight pain in the left thigh.

In this case the symptoms and signs were thought to be so characteristic of a ruptured intervertebral disk that operation was performed despite the fact that lipiodol examination failed to demonstrate any evidence of protrusion of a disk. The history of previous attacks of joint disease that was obtained at the time of the second admission, the x-ray evidence of involvement of the right sacroiliac joint, the elevation of the sedimentation rate and the course following operation indicated rheumatoid arthritis.

In its early stage, rheumatoid arthritis may be diagnosed as psychoneurosis, as in the following case. In the absence of objective findings in the

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hot packs on the knee. The swelling gradually subsided but the stiffness and pain persisted.

Examination in July, 1936 was negative except for the right knee. There was marked thickening of the tissues around this knee and slight tenderness along the joint line medially and laterally. Extension was limited to 10°. The quadriceps muscle showed slight atrophy and moderate weakness. Routine blood and urine examinations were normal. The corrected sedimentation rate was 0.78 mm per minute. Roentgenograms revealed moderate bone atrophy around the right knee, most marked in the subchondral areas. There were slight degenerative changes.

On a regime of increased rest, generalized exercises, hot packs on the right knee and aspirin the pain and stiffness of the knee and the fatigability slowly disappeared. In January, 1937, the patient was free of all symptoms. Slight periarthritic thickening of the right knee persisted, but there was no limitation of extension. The atrophy of the quadriceps had disappeared. She remained well until February, 1938, when slight swelling and pain in the right knee recurred. On resumption of the above regime, the symptoms subsided in a few weeks. In 1940 she had another exacerbation with pain and tenderness in the region of the right sacroiliac joint. There was radiation of the pain down the posterior aspect of the thigh and the lateral aspect of the lower leg. On examination straight leg-raising on the left side was limited to 40°. There was slight hypesthesia over the dorsum of the foot. Pressure on the metatarsophalangeal joints caused slight pain. All symptoms subsided slowly and the patient remained well until March, 1944, when she noticed fatigability, pain and stiffness of the left knee and recurrence of slight pain in the metatarsophalangeal joints.

Examination in June, 1944, showed slight thickening of the tissues around the left knee. Extension was limited to 10° and the knee could be flexed only to 90°. There was slight tenderness of the metatarsophalangeal joints. The patient resumed the regime of rest, exercises, hot packs on the left knee and hot soaks for the feet, aspirin, phenobarbital and added vitamin B complex and was given footplates with support under the metatarsals. She improved slowly and was entirely free of symptoms in January, 1945.

For twenty-eight years the symptoms in this case were characteristic of fibrositis. Subsequently constitutional symptoms appeared and there was evidence of articular involvement. The periarthritic thickening and limitation of motion of the right knee, the elevation of the sedimentation rate and the roentgenographic demonstration of subchondral bone atrophy made it apparent that the patient had rheumatoid arthritis. As might be expected from the fact that there was little evidence of progression during the first twenty-eight years, the disease has been relatively mild, and there have been long periods of complete remission with exacerbations of short duration.

Typical intermittent hydrarthrosis may occur at the onset or in the course of rheumatoid arthritis. The intermittent effusions in such cases resemble in all respects those of idiopathic intermittent hydrarthrosis, being characterized by periodic swelling, recurring with great precision at regular intervals. In our experience most of the patients in whom this characteristic syndrome has occurred have had rheumatoid arthritis. In cases of idiopathic intermittent hydrarthrosis, the appearance of constitutional symptoms, persistent thickening of the involved joints even between attacks and elevation of the sedimentation rate suggest the presence of rheumatoid arthritis.

CASE 11 A 32-year-old priest was admitted to the hospital on March 15, 1937 complaining of intermittent pain and

stiffness of both knees of 5 years' duration. In 1932 he had begun to have recurrent swelling of the knees at regular intervals. In each attack the swelling increased gradually for 3 or 4 days and slowly disappeared in the following 3 or 4 days. The swelling did not involve both knees simultaneously, one usually becoming swollen as the other was returning to normal. During attacks, the knees were uncomfortable but were not extremely painful. Motions were limited because of the effusions. The intermittent hydrarthrosis recurred frequently up to the time of admission. Only during the summer of 1932 had the patient been free of joint symptoms. There had been no weakness or fatigability, no weight loss and no involvement of other joints. The past history and family history were noncontributory.

Examination on admission was negative with the exception of bilateral knock-knee deformities and small effusions in both knees. Routine blood and urine studies were negative. The corrected sedimentation rate was 0.27 mm per minute. Roentgenograms of the knees showed the bilateral knock-knee deformity and some soft-tissue thickening around the right knee. Examination of the synovial fluid showed white-cell counts varying from 1500 to 5000, with a variation in polymorphonuclear leukocytes from 0 to 20 per cent. The concentration of protein in the fluid ranged from 4.5 to 5.5 gm per 100 cc. The mucin in the fluids aspirated during the first few days of the effusions precipitated poorly, but in fluids withdrawn at the end of the attacks the mucin precipitated as a rope mass. Both knees were repeatedly tapped in March and again in June, in an attempt to prevent the recurrent effusions. The patient was treated also with increased rest and hot packs to both knees. On this regime the hydrarthrosis was arrested so that there were no effusions until December 1938. At that time the attacks recurred, presenting the same pattern as previously.

The patient was readmitted on May 4, 1939. Examination of the joints was unchanged. The feet were cool and moist. Routine laboratory studies remained negative. Both knees were again repeatedly tapped. The fluid showed essentially the same findings as in 1937. Following discharge on May 22, the effusions continued to recur at somewhat irregular intervals.

In May, 1940, the patient was readmitted to the hospital. Physical examination remained unchanged with the exception of the fact that there was moderate thickening of the tissues around both knees. The sedimentation rate had risen to 0.49 mm per minute. X-ray examination showed slight atrophy of the bones around the knees. Following discharge on a regime of increased rest and aspirin, the interval between effusions became longer. In 1941, after a period of increased work and emotional stress, the effusions began to come more frequently, occurring in the right knee at regular 2-week intervals.

On readmission in June, 1941 physical and laboratory examinations were unchanged. An attempt to prevent the cyclic recurrence of effusions by repeated aspirations was unsuccessful. On a regime of increased rest, however, the effusions became less frequent and the sedimentation rate returned to normal—0.35 mm per minute.

At many periods during this patient's illness the intermittent effusions recurred with exact regularity and were typical of those of so-called "intermittent hydrarthrosis." The fact that the swelling did not involve both knees at the same time suggests that the factors regulating the amazing regularity of the effusions were active only locally. On several occasions the cycle was altered by a regime of rest and repeated aspirations of the knees, and at one time the effusions disappeared entirely for a period of eighteen months. The gradually progressive involvement of the knees, with periarthritic thickening and x-ray evidence of bone atrophy, indicated rheumatoid arthritis. Relatively slight synovial-fluid abnormalities, with low white-cell counts and few polymorphonuclear leukocytes, only slight alteration of the precipitation of mucin and only

the wrists on the radial side and slight thickening of the knees. The sedimentation rate remained slightly elevated—0.46 mm per minute. X-ray examination of the hands and wrists showed slight atrophy of the bones around the joints. Once again, the attacks became less frequent when the patient worked less hard and resumed her daily rests. During her vacation in the summer of 1945 she became free of all symptoms.

The recurrent attacks of joint pain, swelling, tenderness and redness in this case are characteristic of the palindromic syndrome. Only after the patient had been followed for several years was it possible to make the diagnosis of rheumatoid arthritis. Adequate evidence was then provided by the slowly progressive, chronic joint involvement, with persistent thickening of the tissues around the wrists and knees, the marked constitutional symptoms during exacerbations and the x-ray evidence of bone atrophy. The elevation of the sedimentation rate that was present throughout most of the illness was further evidence in favor of rheumatoid arthritis. The precipitation of exacerbations by infection or periods of overwork or emotional strain was characteristic.

In all cases of rheumatoid arthritis there is some fibrositis, as would be expected from the fact that the fundamental involvement in this disease appears to be that of connective tissue.¹⁴⁻¹⁶ In many early or mild cases the clinical picture is that of so-called "primary fibrositis."¹⁷ This term is used to include a large group of patients whose symptoms consist of general exhaustion and stiffness in joints and muscles that is most apparent in the morning or after resting. In such patients the appearance of objective joint signs, loss of weight or elevation of the sedimentation rate is generally accepted as evidence of rheumatoid arthritis. It is probable that most patients with so-called "fibrositis" have mild rheumatoid arthritis, although in many cases the diagnosis cannot be made until the patient has been observed over a long period of time.

CASE 9 A 25-year-old, married meat packer was admitted to the hospital on October 22, 1940, because of paresthesias, numbness, pain and weakness of the hands of 4 months' duration. In June, 1940, he had noticed increasing difficulty in milking, and soon thereafter numbness and tingling of the hands appeared. He began to experience severe pains in both hands, usually occurring at night and often radiating to the upper arms. The past history was not remarkable except for "rheumatic fever" at the age of 8. On examination, both hands were cool and moist. The 2nd, 3rd and 4th fingers of the right hand and the 3rd and 4th fingers of the left hand could not be completely extended. The palmar fascia seemed thickened and contracted. The subcutaneous tissue on the lateral aspects of the thighs was nodular. Laboratory studies were not remarkable. Blood and spinal-fluid Hinton reactions were negative. The corrected sedimentation rate was 0.22 mm per minute. X-ray examination of the legs, cervical spine, hands and wrists was negative. The muscles of the forearm responded normally to faradic and galvanic currents, and the electromyograms showed a normal pattern. A biopsied specimen of fascia lata showed subacute and chronic inflammation with considerable degeneration of the collagen.

It was concluded that the patient had generalized chronic inflammation of collagenous tissue. He was discharged on October 31, 1940, with a diagnosis of primary fibrositis. Following this, the symptoms improved for 1 week and then

recurred. Two months later he began to have intermittent pain and stiffness in both ankles and hips and the right shoulder. Examination on December 16, 1940, showed generalized lymphadenopathy, tenderness and swelling of the 3rd right metacarpophalangeal joint, periarticular thickening and limitation of motion of both wrists and swelling about the left ankle. The limitation of extension of the fingers was unchanged, as was the granular consistency of the subcutaneous tissues of the thighs. During the following month the joint symptoms became severer and there was increasing fatigability and a loss of 5 pounds in weight.

The patient was readmitted to the hospital on March 18, 1941. Examination remained as in December, 1940. Routine urine and blood studies were normal. Brucella agglutination tests were negative. The corrected sedimentation rate was 0.18 mm per minute. X-ray examination showed slight decalcification of the bones around the right wrist.

On a regime of complete bed rest, generalized exercises and aspirin the patient improved, and at discharge on June 13 he had only slight stiffness of the hands and ankles. One month later, however, he began to have increasing joint pain, involving especially the right ankle and both wrists. There was occasional pain in the right temporomandibular joint. Motion of the right ankle became extremely limited, and a valgus deformity of the foot developed associated with peroneal spasm. The right knee and the metacarpophalangeal and midphalangeal joints of both hands showed periarticular thickening. The sedimentation rate rose to 0.44 mm per minute. The prepatellar bursa appeared to be thickened and was biopsied on January 21, 1942. Microscopic examination showed chronic inflammation and fibrosis.

The symptoms persisted without much change until April, 1942, when the patient began to improve, and in 1943 he became free of all symptoms except pain in the right ankle. Periarticular thickening of the wrists, metacarpophalangeal joints and right ankle persisted. During the last 2 years he has had only slight fatigability and has been able to work regularly. He has continued to have slight pain in the right ankle and in the 2nd and 3rd metacarpophalangeal joints. Examination in October, 1945, showed thickening of the tissues around these joints. X-ray examination revealed slight atrophy of the bones of the right ankle.

The symptoms and signs during the early stage of the disease in this case suggested a widespread involvement of the connective tissue. The examination of the tissue removed from the thigh corroborated this impression and led to a diagnosis of fibrositis. The subsequent progressive involvement of many joints with periarticular thickening and x-ray evidence of decalcification of bones, the fatigability, the weight loss and the elevation of the sedimentation rate indicated rheumatoid arthritis.

In the following case, a less severe, more frequent form of fibrositis represented the onset of rheumatoid arthritis. In this milder form the disease remains active, although relatively stationary, for many years, and then slowly progresses and presents characteristic manifestations of rheumatoid arthritis.

CASE 10 A 62-year-old, unmarried housekeeper was first seen on July 10, 1936, because of pain and stiffness of the right knee of 2 months' duration. Thirty years previously she had noticed occasional stiffness in various joints and in the muscles of the legs. This gradually became more marked, especially in the knees, and occurred each morning and whenever she had been sitting still for a long period of time. In 1926, she began to experience occasional numbness in the feet and occasional pain under the metatarsophalangeal joints. Arch supports were worn with some relief. In 1935 she began to tire easily. In May, 1936, while riding in an automobile she noticed that her knees were unusually stiff. At the end of the ride she had difficulty in starting to walk, and within a few hours the right knee became swollen and painful. She consulted a physician, who advised the use of

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NEW HAMPSHIRE MEDICAL SOCIETY

Proceedings of the One Hundred and Fifty-Fourth Anniversary

THE scientific sessions of the one hundred and fifty-fourth anniversary of the New Hampshire Medical Society were opened at the Hotel Carpenter, Manchester, at ten o'clock on the morning of May 15, 1945, with President Fred Fernald, of Nottingham, presiding.

The first item on the program was a motion-picture film "Surgical Treatment of Varicose Veins and Ulcers," presented through the courtesy of Davis and Geck, Incorporated. This was followed by a paper by Dr. Henry H. Amsden, of Concord, the subject being "Epistaxis." Dr. John Milne, of Hanover, then presented a paper entitled "Infectious Mononucleosis." A paper "How Can Physicians Help Lawmakers?" was then given by Dr. Joseph S. Lawrence, director of the Washington Office of the Council on Medical Service and Public Relations, American Medical Association. This was discussed by Mrs. John Sargent, of the New Hampshire Farm Bureau Federation, and by Mr. James McElroy, of the New Hampshire Manufacturers' Association. The morning session was concluded by remarks by Mr. James M. Langley concerning the responsibilities of the recently appointed state commission to study hospital and health facilities in New Hampshire.

The afternoon session opened with the awarding of fifty-year certificates to Dr. Anna M. Littlefield, of Laconia, Dr. William H. Mitchell, of Loudon, and Dr. Henry L. Stickney, of Boston. Dr. Stickney, on receipt of his certificate, spoke as follows:

I accept this honor and distinction, and I find that words are inadequate to express my great gratification for the fifty years that I have been a member of this society. I believe that I have missed only two meetings in all that time, these being when I was in the A.E.F. during World War I. I have profited much by the papers that have been read here. I realize that I have not contributed so much as I should have liked, in a scientific way, to the Society, indeed, I feel that I have been a liability rather than an asset.

But, I want to tell you that I have appreciated the fellowship, the close companionship of my fellow members through all these years and I hope that I may see you in 1970. I shall repeat General MacArthur's statement to the effect that "I shall return" in twenty-five years and hope to receive another designation, if one is available.

Dr. Fernald then presented the president-elect, Dr. Richard W. Robinson, of Laconia, who spoke as follows:

One would not be human if one did not feel a little bit puffed up and flattered by the honor that the House of Delegates has conferred on me by electing me as your president.

For a long time, I have felt a great deal of personal sorrow because of the fact that John Gile, of Hanover, has not been well. To that feeling of sorrow is added a feeling of regret, for your sake, because if he had been well, your leadership this year would have been more efficient and better.

But the fact is, of course, that the immediate path that lies ahead of organized medicine today is through the deepest of jungles, beset by many hidden pitfalls, and this year you will see walking ahead of you a pair of very big shoes on a pair of very small feet, and I only ask those who walk behind me, when they see the shoes steering off the straight and narrow, to do me the favor of kicking them into line.

I beg your co-operation and help, and I promise you that I will do the best I can. The way has been made easier by the competent administration of Fred Fernald, and I want to thank him personally for lightening the load in that way.

The report of the Trustees was given by Dr. H. N. Kingsford.

FINANCIAL REPORT OF THE TRUSTEES FOR THE YEAR ENDING DECEMBER 31, 1944

Receipts

Interest on various deposits	\$782 12
Interest on United States Series G Bonds, other than those in Benevolence Fund	456 25
Contributions to Benevolence Fund	913 25
Total receipts	\$2,151 62

Expenditures

Expenses of Society as voted	1,859 66
Burnham prizes	150 00
Total expenditures	\$2,009 66

* * *

GENERAL FUND

Deposits New Hampshire Savings Bank	3,152 98
Portsmouth Trust and Guarantee Company	1,223 90
Nashua Trust Company	398 23
United States Defense Bonds, Series G	3,000 00
	\$7,775 11

BARTLETT FUND

Deposits Portsmouth Savings Bank (\$352 11 of this is a permanent fund, the income to be expended only for the benefit of medical science, as may be directed by vote of this society)	2,998 92
United States Defense Bonds, Series G	2,000 00
	\$4,998 92

PRAY FUND

Deposits Strafford Savings Bank (\$1000 00 of this is a permanent fund, the income to be expended only for prize essays)	291 08
United States Defense Bonds, Series G	1,000 00
	\$1,291 08

moderate elevation of the protein content are occasionally found in mild rheumatoid arthritis

* * *

The above examples of some of the manifestations of rheumatoid arthritis indicate that both the onset and course vary greatly in each case. These variations produce difficulties in making the diagnosis, estimating the prognosis and evaluating the treatment.

Diagnosis in early or atypical cases is often impossible until the patient has been under observation for a long period of time and more typical features of the disease have appeared, as in Cases 5, 8, 9, 10 and 11. Such a situation is unfortunate, since early recognition makes it possible to start treatment at a time when it is most effective. It is generally agreed that whatever the type of therapy employed, patients treated early in the course of their disease usually do much better than do those with cases of longer duration.

The exact prognosis in any individual case usually cannot be determined, but it is obvious from cases exemplified by the above reports that there may be complete remissions lasting for many years, as in Cases 2 and 3.¹⁸ It seems probable that some patients have only one attack without subsequent exacerbation—that, for instance, the remission in a case like Case 4 may last throughout life. In moderately severe cases, the patient tends to have recurrent exacerbations and remissions with varying degrees of incapacitation. There remain a small percentage of cases in which the disease is extremely severe and progresses without remission despite therapy.

Treatment does appear to hasten remission and in some cases to prevent exacerbations. The variations in the course of the disease, however, make evaluation of the effect of therapy impossible unless one follows a patient over a long period of time both before and after treatment. The tendency of the disease is to remit, and if therapy of any type is instituted at the beginning of a natural remission, a false impression of the value of that treatment is obtained. It is chiefly for this reason that the results of so-called "specific cures" vary so greatly from clinic to clinic. The value of the major features of treatment is, however, generally accepted, despite the persistent disagreement concerning the relative usefulness of more specific types of therapy, such as gold. There is general agreement on the importance of bed rest to the extent indicated by the severity of the disease, reduction of emotional tension so far as possible, generalized exercises to improve or maintain muscle and joint function, proper support for joints to allow reduction of spasm and pain and prevent deformities, application of heat to actively involved joints, adequate analgesia and an adequate supply of all the essential elements of nutrition with additional vitamin A, vitamin B

complex, vitamin C, iron and transfusions when necessary.¹⁹⁻²¹ Sulfonamides⁸ and penicillin²² have been shown not to alter the course of the disease.

A factor of fundamental importance in the treatment of rheumatoid arthritis is the realization that treatment of chronic disease is different from that of diseases of short duration, and requires a different point of view on the part of both physician and patient. Instead of a constant hope for a dramatic change and repeated attempts to produce a sudden improvement, there must be an appreciation of the nature of the disease, of the importance of the present treatment for final healing and of the value of all parts of the regime. More emotional stability and more rapid improvement would result and fewer so-called "cures" would be proffered if the daily or weekly fluctuations of symptoms were realized to be of little significance and if no attempt were made to ascribe all changes entirely to recent alterations in activities, diet or medication.

Proper treatment of rheumatoid arthritis necessitates even more consideration of the patient as a human being than is necessary in acute diseases. Attention must be given not only to the many psychogenic factors that played a role in the precipitation and progression of the arthritis but also to the various problems produced by the disease. There must be a realization that whatever emotional instability previously existed is increased by the illness. The effect of the financial load caused by the sickness and of the disruption of activities and of plans must be handled. At all times an attempt must be made to understand what the patient thinks about the disease, to be aware of and lessen his fear of it and to increase his insight into the effect of psychogenic factors on the course of the disease.

This survey of the varied manifestations of rheumatoid arthritis indicates that a large number of mild, atypical cases occur in addition to the many typical and usually severer cases. It becomes apparent that rheumatoid arthritis is an extremely frequent disease and that many more cases are mild than is generally believed. Only when this situation is more generally realized can the diagnosis of arthritis become less disturbing to physician and patient.

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is deviation, a PR interval of 0.14 second, upright T_1 and T_2 , a slightly inverted T_3 , an inverted P_3 , an upright T wave and an absent S in Lead CF_2 and inverted T waves in Leads CF_1 and CF_2 . A urine culture on a catheterized specimen showed abundant growth of colon bacilli. A blood Hinton test was negative.

At times the patient complained of pain in the flanks and burning on urination. She was given sulfathiazole, Hykinone and intravenous injections of 10 per cent dextrose. She also had episodes of generalized cramping abdominal pain but passed light-brown feces and gas. The abdomen continued to be distended and tympanitic.

On the eleventh hospital day the patient had a sudden chill, with pain in the right upper quadrant and the temperature rose to 101°F . The abdomen became tender, and peristalsis diminished. On the following day, however, she felt much better and passed gas freely by rectum. A paracentesis was performed, and 4000 cc of clear, yellow fluid was removed, this had a specific gravity of 1.010 and contained 50 white cells and 50 red cells per cubic millimeter. A pelvic examination revealed a smooth, patulous cervix and an irregular enlargement of the uterus to the right. Neither ovary could be distinguished. There were no masses in the vaults. The liver and spleen were not palpable.

On the day after the paracentesis she had a severe attack of cramping midepigastria pain, which was accompanied by nausea and the vomiting of strongly guaiac-positive coffee-ground fluid. At that time the abdomen was distended and tender, with sluggish peristalsis. She went slowly into coma, and marked dependent edema appeared. It subsided after the amount of fluid given intravenously had been reduced. She expired on the twenty-second hospital day.

DIFFERENTIAL DIAGNOSIS

DR. WADE VOLWILER. This elderly woman apparently suffered from an extremely "sick" liver and was subjected to an almost too complete investigational scrutiny, the latter turned up a museum of pathology, most of which appears to be of little consequence as regards her fatal illness. We are first presented with the characteristic nutritional history of a person with alcoholic cirrhosis, a disease that may be purely one of nutritional deficiency. All the liver-function studies were compatible with a severely and diffusely damaged liver and intrahepatic jaundice. The albumin-globulin ratio was 0.76. It has been shown that the albumin fraction drops faster than the globulin fraction in protein deprivation, but strangely enough we are told that this patient was well developed and nourished. I suppose that, if a person eats a starvation diet but consumes adequate alcohol for energy calories, the fat stores of the body are not depleted to the extent that the protein reserve is. I do not believe that we see an albumin-globulin ratio below 1.0 in the

hypoproteinemia of protein starvation, without the added presence of damage to the liver parenchymal cells or in the nephrotic syndrome.

As is often true in cirrhosis, the degree of jaundice was not a true index of the severity of the liver damage. The markedly prolonged prothrombin time was an exceedingly ill omen initially. No statement is made whether it responded to parenteral vitamin K-derivative supplements, but I am reasonably certain that it responded only feebly. It is impossible clinically to say whether the liver disease in this case represented an acute exacerbation of a chronic cirrhosis or an infectious hepatitis superimposed on a chronic alcoholic cirrhosis. The absence of varices does not rule out a chronic cirrhosis. Since the abdomen was always distended, an enlarged spleen could have easily been missed, but it must have been enlarged. The ascitic fluid was a bile-stained transudate. The various types of abdominal pain described are often seen in acute hepatitis. There may be peristaltic disturbances varying from bursts of the hyperactive normal-pitched variety, producing diarrhea, to a paralytic ileus in acute cases, producing marked tympanitic abdominal distention. Ascites and hypoproteinemia with edema of the bowel wall interfere considerably with normal bowel action.

If we can believe the physical findings regarding the position of the liver edge, this organ diminished somewhat in size during the twenty-two hospital days, probably owing to a destruction of parenchymal cells. The gradual lapse into coma is typical of a cholemic death.

The source of the guaiac-positive vomitus is purely speculative. I should suppose that there was a chronic alcoholic gastritis. The hiatus hernia was really too small to have caused symptoms or to have been the site of localized gastritis. Superficial ulcerations of the lower esophagus in cases of fatal infectious hepatitis have been described. Spontaneous hemorrhage from a marked hypoprothrombinemia is possible but not likely. Duodenal diverticula are usually incidental findings of no consequence.

The patient had a colon-bacillus urinary-tract infection, and the absence of albuminuria indicates that it was chiefly a cystitis. I should like to ascribe the single chill to an extension of this infection, with a possible transient bacteremia at that time.

The sigmoidal spasm noted fluoroscopically during the barium enema suggests a mild diverticulitis in addition to the extensive diverticulosis. Clinically this seems unimportant, it may have contributed to the periodic diarrhea and crampy abdominal pain.

The areas of increased density in the right lower lobe could have been due to a mild bronchopneumonia in this debilitated patient, but they were probably areas of atelectasis resulting from a high diaphragm and poor aeration.

BURNHAM FUND

Deposits New Hampshire Savings Bank (\$1,140 00 of this is a permanent fund, the income to be expended only for prize essays)	1,064 01
United States Defense Bonds, Series G	1,000 00
	<hr/> \$2,064 01

BENEVOLENCE FUND

Deposits New Hampshire Savings Bank (\$688 87 of this is accrued income available for the purposes of the fund)	3,239 81
United States Defense Bonds, Series G	3,000 00
	<hr/> \$6,239 81

GEORGE C WILKINS, M D
SAMUEL T LADD, M D
HOWARD N KINGSFORD, M D, *Secretary*

The Secretary, Dr Carleton R Metcalf, then presented the report of the House of Delegates

Following introductory remarks by Dr L K Sycamore, Mr Russell S Spaulding, executive secretary of the Blue Shield, spoke concerning its excellent progress and various problems

The first paper of the afternoon, "Surgical Treatment of Hypertension," was given by Dr Reginald H Smithwick, of Boston "Reconstructive Surgery of the War Wounded," by Dr Philip D Wilson, of New York City, was read by Dr Wilson's associate, Dr John R Cobb Dr Alfred L Frechette, of Concord, then presented a paper entitled "Medical Relief Problems in Africa"

Dr W J P Dye then read certain proposed changes in the constitution and by-laws of the Society that were to be acted on at the next meeting of the House of Delegates

The scientific sessions were adjourned at 5 30 p m

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor**

BENJAMIN CASTLEMAN, M D, *Acting Editor*

EDITH E PARRIS, *Assistant Editor*

CASE 31471

PRESENTATION OF CASE

A seventy-two-year-old woman entered the hospital complaining of abdominal distention

Eight weeks before admission the patient fell out of bed and "collapsed" After this episode she noted the onset of jaundice, progressively increasing abdominal distention, anorexia and brown, foul-smelling urine The stools were light brown Three weeks before admission she had one episode of vomiting

The past history was negative except that for many years she had drunk a glass or two of hard liquor daily During the few months before admission she had not eaten much food Thirty years before admission she had had a right mastectomy for cysts

The patient was well developed and nourished and moderately jaundiced A right mastectomy scar was present The lungs were clear, but the diaphragm was elevated, with limited excursions The heart was normal except for an apical systolic murmur The abdomen was protuberant and tympanitic Shifting dullness was present in the flanks, with an equivocal fluid wave The liver

was enlarged two fingerbreadths below the right costal margin The lower legs were edematous

The temperature was 99°F, the pulse 80, and the respirations 20 The blood pressure was 125 systolic, 80 diastolic

The urine contained no albumin but many white cells, it was positive for urobilinogen in a dilution of 1:128 The red-cell count was 3,900,000, with a hemoglobin of 12 gm The white-cell count was 5500, with 73 per cent neutrophils The nonprotein nitrogen was 20 mg per 100 cc, and the total protein 5.1 gm, the albumin being 2.2 gm and the globulin 2.9 gm The serum phosphorus was 3.5 mg per 100 cc, and the alkaline phosphatase 61 units A cephalin flocculation test was + in twenty-four hours and ++++ in forty-eight hours The prothrombin time was 38 seconds (normal, 20 seconds) The van den Bergh reaction was 4.6 mg per 100 cc direct and 6.1 mg indirect An x-ray film of the chest showed clear lung fields The right half of the diaphragm was high, and the left costophrenic sinus was blunted The heart, aorta and upper mediastinum were within normal limits The bones of the lumbar spine and pelvis were normal Three days later, at the time of a barium swallow, the right lung showed areas of increased density in the lower lobe The esophagus was moderately curled, but there were no varicosities A hiatus hernia measuring 5 by 3 cm was seen There was a small diverticulum arising from the upper inner aspect of the second part of the duodenum, and a larger one somewhat below it A barium enema revealed some spasm of the sigmoid and multiple diverticula in the sigmoid and descending and transverse colon An intravenous pyelogram was negative Above the bladder was a 12-by-10-cm pelvic mass, which was of homogeneous density and not calcified An electrocardiogram showed normal rhythm at a rate of 100, left-

*On leave of absence

were essentially normal and the spleen was not enlarged. The uterus was slightly enlarged and contained several 1-cm subserous calcified fibroids. The heart was normal, and the lungs were congested and edematous in their dependent portions. The liver weighed 750 gm, having shrunk to half its normal size. The capsule was wrinkled and raised by many small bright-yellow nodules. Section through the parenchyma showed a dull-green background, which was homogeneous except that small yellow nodules were concentrated in various portions. These were sometimes confluent to form nodules over 2 cm in diameter.

Microscopically, sections of the green areas showed complete destruction of the pre-existing liver cells,

duct epithelium or liver cells. When the tubules happened to be cut in longitudinal section the two types were often seen to merge one with the other. This brings up the old and unsettled question whether bile-duct epithelium can be transformed into liver cells. Many of the tubules contained bile casts.

Sections from the yellow areas showed the formation of atypical lobules separated by bands of condensed stroma (Fig 2). These regenerating liver cells were arranged in broad compact cords that did not converge toward a central vein. They were separated by sinusoids that contained only a few blood cells. There was fatty change in the new liver cells.

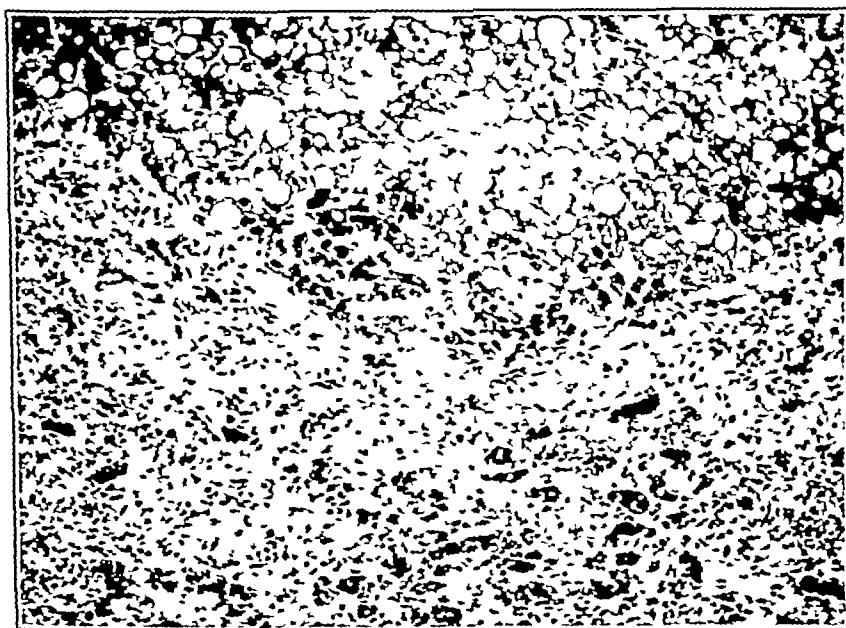


FIGURE 2 Photomicrograph of a Yellow Area in the Liver

leaving behind the normal portal structures and small perlobular bile ducts as landmarks (Fig 1). The reticular framework was collapsed and infiltrated by lymphocytes, plasma cells and a few polymorphonuclear cells. In the reticulum between the portal triads there were regenerating cells that lay singly and in small groups and often formed cords and tubular structures. The cells lining these tubules were of two types, resembling either bile-

This is the picture of subacute yellow atrophy similar to that seen in epidemic hepatitis. I do not believe that the patient had a pre-existing cirrhosis, since all the findings can be accounted for by an acute hepatitis with attempts by the parenchyma to regenerate.

So far as we are aware the patient had not ingested a hepatotoxin, other than the possible inclusion of alcohol in this category.

CASE 31472

PRESENTATION OF CASE

A fifty-eight-year-old woman entered the hospital complaining of constipation.

About ten months before admission she first noticed difficulty in moving her bowels, even with strong laxatives. The stools were usually formed

but never bloody or tarry. She had had occasional episodes of diarrhea. She had also had "indigestion," flatulence and anorexia. During the month before admission she had lost 17 pounds and had become weak. She had had no nausea, vomiting or abdominal pain. For an indefinite length of time she had had exertional dyspnea, without orthopnea or ankle edema.

There were no real signs of cardiac failure. The electrocardiogram is compatible with a transverse position of the heart, except for the inverted T waves in the chest leads, which indicate coronary-artery disease.

The pelvic mass revealed in the intravenous pyelogram probably corresponds to the fibroid uterus felt during the pelvic examination.

May we see the x-ray films?

DR CLAYTON H. HALE: The only films of the upper intestinal examination are these spot films of the lower esophagus and the second portion of the duodenum. The hernia can be seen quite well. Of course, the examiner had a better chance to make a diagnosis of varices than I have, but from the films alone I should think that there is a sug-

as I should like to see it. One is not justified in making a diagnosis of hepatoma from this film.

DR VOLWILER: My diagnosis is chronic alcoholic cirrhosis, with a superimposed acute exacerbation.

CLINICAL DIAGNOSES

Portal cirrhosis
Cystitis
Leiomyomas of uterus

DR VOLWILER'S DIAGNOSES

Chronic alcoholic cirrhosis, with superimposed acute exacerbation
Cystitis
Pulmonary atelectasis
Leiomyomas of uterus

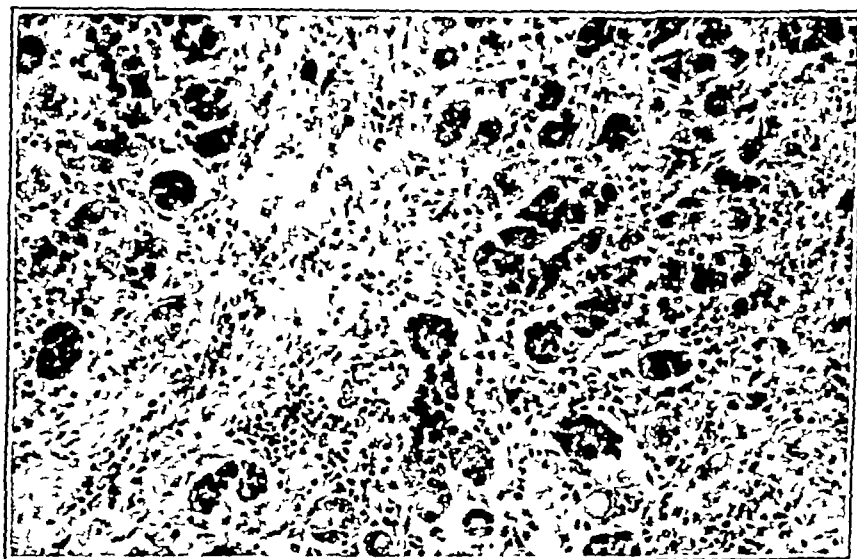


FIGURE 1 Photomicrograph of a Green Area in the Liver

gestion of varices. They might have been air bubbles, but the waviness in this area can be interpreted as curling. There is a suggestion of small defects in that region, but they are questionable. Here is the diverticulum in the duodenum that was described. The barium-enema film shows many diverticula and the area of spasm that was described, with undoubtedly some swelling of the mucosa. I can make out no definite enlargement of the liver and spleen in any of these films. The right half of the diaphragm is elevated, and there is a hump in it that is somewhat confusing. The chest film shows old adhesions at the left costophrenic sinus. The mass that was palpated in the pelvis can be seen in this film; it is perfectly consistent with a large fibroid uterus.

DR VOLWILER: I suppose that Dr. Hale wants me to say that a hepatoma was the cause of the hump in the diaphragm.

DR HALE: I only wanted to mention it. It is not so localized to a small portion of the diaphragm

ANATOMICAL DIAGNOSES

Subacute yellow atrophy of liver
Icterus
Ascites
Pulmonary congestion and edema
Peripheral edema
Diverticula of colon and duodenum
Cystitis
Leiomyomas of uterus

PATHOLOGICAL DISCUSSION

DR RONALD C. SNIFFEN: At the time of death the patient was mildly jaundiced, with a generalized pitting edema. The peritoneal cavity contained 2000 cc of clear straw-colored fluid. As described in the clinical summary, diverticula were present in the colon and duodenum, and the esophageal hiatus was enlarged; there was no diverticulitis. The entire gastrointestinal tract showed mucosal congestion. A mild cystitis was present; the kidneys

ings, and limit the discussion to four possible diagnoses. They are carcinoma of the sigmoid, diverticulitis of the sigmoid, regional enteritis and carcinoma of the ileum.

Of the various means we have in arriving at a diagnosis probably the history is the most valuable in this case. As we read it, we learn that the patient was a woman of fifty-eight years. I hesitate to say that she was an old person, but at least she was out of the age group of regional enteritis and more apt to be in that of cancer of the sigmoid or of diverticulitis. The first symptom was difficulty in moving the bowels. That, of course, is a rather unusual symptom for a primary lesion in the small bowel. Such lesions are usually ushered in with attacks of diarrhea or upper abdominal cramps. Increasing constipation is the typical first symptom of carcinoma of the sigmoid. It is also important to note that constipation had been present for ten months before she entered the hospital. This chronic constipation is not entirely characteristic of diverticulitis of the sigmoid. Constipation is occasionally noted as a symptom, but diverticulitis is apt to begin more dramatically, with either a sudden pain in the lower abdomen or a sudden attack of diarrhea that subsides and then recurs. From the first symptom I am therefore inclined toward a diagnosis of carcinoma. The stools were never bloody. Blood is usually present if the patient has carcinoma. Episodes of diarrhea are often found in the presence of carcinoma of the sigmoid or in that of the other diagnoses that I have mentioned. I am surprised by the presence of "indigestion" and by the lack of nausea, vomiting and abdominal pain. I take it that she had a trace of one or more of the last three symptoms, although they were extremely minor.

To proceed to the physical examination, there is evidence of slight anemia, dehydration and infection, the last apparently arose from an abscess, with or without an underlying tumor, in the left lower quadrant. In the presence of obstruction it is strange that peristalsis was entirely normal. I should like to know about the rectal examination. I can infer that it was negative, because one done several days later is so recorded.

DR. RONALD C. SNIFFEN: The rectal examination was negative, except for tenderness.

DR. WELCH: Proctoscopic examination might have been of some interest, but it would have been attended with a definite hazard in this patient because perhaps she had already perforated the bowel.

So far as the laboratory work is concerned, there is not much of interest except for the x-ray examination. Since the stools are not recorded, I assume that bloody stools were not noted. She might have had them at some time before entry, or even while in the hospital. X-ray studies are apt to be unsatisfactory in such a case, — a sick patient does not tolerate palpation of the abdomen or a large

amount of barium, — but we had better look at the films to see if they can give us any help.

DR. CLAYTON H. HALE: This oblique projection best demonstrates the area of narrowing. This is the shelf-like defect, which begins 2 cm. above the rectosigmoid junction. There is no evidence of normal mucosa over this area of narrowing in the sigmoid, which suggests an intrinsic lesion in the sigmoid. One has to be careful, however, since narrowing from any cause tends to distort the mucosa. I presume that this is the film suggesting the fistula into the ileum. The fact that there is a fistula into the ileum is in favor of primary disease in the colon and not of metastatic disease, such as one would see from an ovarian carcinoma, which produces an extrinsic mass. The length of the lesion is a little unusual for a carcinoma, this makes one think of lymphoma, although we have seen quite a few carcinomas of this length.

DR. WELCH: To return to the four diagnoses considered at the outset, I shall rule out carcinoma of the ileum because of the long history and because the x-ray films look much more typical of a primary lesion in the large bowel with secondary involvement of the ileum. I shall rule out regional enteritis on the basis of the facts mentioned above. This leaves carcinoma of the sigmoid and diverticulitis as well as Dr. Hale's suggestion of lymphoma. There is no additional evidence for lymphoma in the way of enlarged nodes or an enlarged spleen. I am not sure, but I believe that lymphoma is likelier to produce uniform involvement of all layers of the bowel wall, without perforation of the colon. So far as diverticulitis versus carcinoma is concerned, for the reasons that I have listed above in the discussion of the history and because of the fact that the x-ray findings, although not typical, are consistent with the diagnosis of carcinoma, I shall make that my diagnosis — carcinoma of the sigmoid, with perforation into the ileum and intra-abdominal abscess.

CLINICAL DIAGNOSIS

Carcinoma of sigmoid, with ileocolic fistula

DR. WELCH'S DIAGNOSIS

Carcinoma of sigmoid, with perforation into ileum and intra-abdominal abscess

ANATOMICAL DIAGNOSES

Adenocarcinoma of sigmoid, with extension to ileum

Ileocolic fistula, with local abscess formation

Perforation of transected ileal loop

Acute fibrinopurulent peritonitis, generalized

Pulmonary infarction

PATHOLOGICAL DISCUSSION

DR. DEAN CRYSTAL: Laparotomy revealed a loop of ileum, 10 cm. from the ileocecal valve, that was

The menopause had occurred seven years before admission. She had had occasional frequency of urination, as well as nocturia.

The patient was well developed and well nourished but pale and lethargic. The tongue was dry. The heart and lungs were normal, except for an early, short, blowing Grade I systolic murmur over the aortic area. The abdomen was distended and tympanitic, with generalized voluntary muscle spasm. In the left lower quadrant there was tenderness over a nonmovable mass, which was dull to

be a shelf, with abrupt narrowing, extending for 9 cm., and an irregularity of the mucosa that was suggestive of ulceration (Fig 1). There was marked edema in this area, and a small fistula was seen to lead into the ileum. The entire examination could not be done because of difficulty in getting the barium beyond the area of narrowing. No diverticula were seen.

The patient continued to run a temperature as high as 105°F. She was given intravenous dextrose in water and 12 gm of sulfasuxidine a day. A Miller-



FIGURE 1 Roentgenogram of Barium Enema Showing the Area of Narrowing in Sigmoid and the Ileocolic Fistula (arrow).

percussion, the mass apparently originated in the pelvis. Peristalsis was normal. The liver was palpable two fingerbreadths below the right costal margin.

The temperature was 103°F, the pulse 70, and the respirations 20. The blood pressure was 110 systolic, 75 diastolic.

The blood showed a hemoglobin of 80 per cent. The white-cell count was 14,500. The urine was negative except for many white cells in the sediment. An x-ray film of the chest showed a normal heart and lungs. A barium enema reached just beyond the rectosigmoid junction, where there appeared to

be a shelf, with abrupt narrowing, extending for 9 cm., and an irregularity of the mucosa that was suggestive of ulceration (Fig 1). There was marked edema in this area, and a small fistula was seen to lead into the ileum. The entire examination could not be done because of difficulty in getting the barium beyond the area of narrowing. No diverticula were seen.

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DIFFERENTIAL DIAGNOSIS

DR CLAUDE E. WELCH This is essentially the problem of a lower abdominal mass associated with an ileosigmoidal fistula, infection and intestinal obstruction. I am going to throw all caution to the winds, a dangerous procedure at one of these meet-

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HEALTH SUPERVISION OF THE SCHOOL CHILD

TO DETERMINE the need for health supervision of the school child with as great a degree of scientific accuracy as at the present seems possible, Jean Downes* has reported a survey made under the auspices of the Milbank Memorial Fund. This study was aimed chiefly at finding out how far sickness may be used as an index of that need.

White families living in thirty-five city blocks in the Easton Health District of Baltimore were selected for the study. One part of the report deals with the illness experienced during a twelve-month

*Downes J. Sickness as index of need for health supervision of school child. *Am J Pub Health* 35:593-601 1945

period by the 1060 children of school age in these families, the other part analyzes the data from families observed three to five years.

The conclusion that, for the individual child, frequency of attacks of illness — excluding communicable diseases, infectious skin conditions and tonsillectomies — can serve as a means of selecting children who are most in need of health supervision does not seem unexpected, nor does the observation that those having two or more attacks of illness were found to have the greatest chance of experiencing bed or disabling illnesses refute the experience of most practitioners.

Further conclusions are that siblings of a child selected because of two or more attacks of illness had much higher attack rates over a period of three to five years than did those of a child with a better health record, that families varied greatly with respect to illness of the school-age child and that individual children tended to remain at about the same sickness level over a period of five years. The final conclusion is that the health of the school child presents a problem concentrated in certain families, thus suggesting that the family rather than the child alone should be the focal point for health supervision.

It is beside the point to say that the family doctor and his counterpart, the pediatrician, have long been aware of the general truth of the author's conclusions. A study that demonstrates these points with statistical accuracy helps to confirm what could otherwise be accepted only as impressions, furthermore, it brings this information to the agencies where it can be used in a practical manner.

We have been reawakened, partly by the experiences of Selective Service, to the need of better health supervision of the school child, here is a study that will help give direction to that study.

MARION SIMS AND HIS SILVER SUTURES

Sims's¹ paper, published in 1852, on the treatment of vesicovaginal fistula, which describes his operation to cure this distressing condition, is one of the outstanding landmarks of American medical history. Superbly written and illustrated with twenty-two excellent woodcuts, few original procedures have

adherent to a huge pelvic mass, including the sigmoid. Presumably this represented the fistula.

Our reasoning was that the fistula itself should provide decompression of the affected loop of ileum; that is, it would remove the mucous and enteric secretions. Accordingly the ileum was transected above and below the fistula and the ends inverted. Continuity of the ileum was re-established by an end-to-end anastomosis.

To defunction the diseased large bowel in the pelvis a transverse colostomy was performed. By these two maneuvers we were able, as a first stage, to sidetrack completely the fecal stream from the fistula. The feasibility of resection of the patient's lesion, en bloc, was to await appraisal as she improved.

DR SNIFFEN: Later a proctoscopy was done, nothing conclusive being found except that the stricture seemed to be due to an extrinsic mass. They also removed what looked like a chicken bone.

The patient did not do well postoperatively. She went into moderate circulatory collapse, since it was thought that she had developed pulmonary infarction, the superficial femoral veins were tied. She then went into profound circulatory collapse and died.

At autopsy this patient had a generalized fibrinopurulent peritonitis. A colostomy had been performed in the transverse colon. Ten centimeters proximal to the ileocecal valve, a 25-cm segment of ileum had been isolated and turned in at both ends and the continuity of the small intestine had

been restored by an end-to-end anastomosis. All suture lines were intact. The isolated loop of ileum was adherent to the sigmoid, rectum and other pelvic organs, and a 2-mm acute perforation was present in its midportion on the anterior surface. This had led to the generalized peritonitis. On opening the loop of ileum a fistula 1.5 cm in diameter was found that led into the closely adherent sigmoid. Dissection of the rectum and sigmoid disclosed a 2-cm annular tumor at the rectosigmoid junction, with almost complete obliteration of the lumen at that point. An extension of the tumor proximally formed an ulcer crater 7 cm in diameter, and the fistulous opening lay in the depths of the crater. There were also small abscesses in the local soft tissues. The tumor was an adenocarcinoma.

In addition the patient had pulmonary congestion and edema, and the main artery to the left lower lobe contained a 3-cm ante-mortem embolus. The latter was recent and had produced early infarction in the lower lobe.

DR ARTHUR W. ALLEN: Can the chicken bone be seen on the x-ray films?

DR HALE: I cannot see any foreign body.

DR CRYSTAL: The service discussed this patient after her death. We thought that the chicken bone was an incidental finding. Our great regret was failure to provide a vent for the blind loop of ileum, which we erroneously assumed would decompress through the fistulous tract visualized by x-ray examination and confirmed at autopsy.

on was a complete success. The sutures were made of gilded silver, and Gosset stated that silver had the advantage of exciting little irritation and did not introduce ulceration with the same rapidity as silk or any other material. Apparently Gosset had used these sutures on a variety of occasions other than vesicovaginal fistula with uniform advantage, and the article appears to indicate that the procedure was in use long before 1834.

Sims's claim, therefore, that he was responsible for "the greatest surgical achievement of the nineteenth century" cannot be accepted in the light of historical facts as they are known today. It is quite likely, however, that Sims was unaware of the previous work in London. In fact, Gosset's work might well have been completely ignored were it not for a pamphlet carefully preserved in a medical library, with a notation of importance by the owner. Such is the way that medical history is sometimes made.

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MASSACHUSETTS MEDICAL SOCIETY

DEATHS

MACLEOD — John M. MacLeod, M.D., of Quincy, died October 19. He was in his seventy-third year. Dr. MacLeod received his degree from McGill University Faculty of Medicine, Montreal, in 1906. He was censor of the Norfolk South District Medical Society for 1925 and 1926. He was school physician in Quincy for 1935 and 1936 and city physician from 1942 to 1945. For the past twenty years he had been a member of the staff of the Quincy City Hospital. His widow and two sons survive.

MCCAUSLAND — William J. McCausland, M.D., of Quincy, died November 5. He was in his seventy-first year. Dr. McCausland received his degree from Harvard Medical School in 1900. He was a fellow of the American Medical Association and a member of the American College of Physicians. His widow survives.

SILBERT — Harry Silbert, M.D., of Salem, died October 31. He was in his fiftieth year. Dr. Silbert received his degree from Tufts College Medical School in 1921. Prior to going to Salem in 1924 he served on the staff of the State Hospital in Middleboro and the Lying-In Hospital in New York City. He was appointed Salem city physician in 1929, and served for several years. His widow, a daughter and a son survive.

STRATTON — Charles W. Stratton, M.D., of Lee, died November 6. He was in his seventieth year.

Dr. Stratton received his degree from Albany Medical College in 1905.

A daughter, a son, a sister and a grandson survive.

COMMITTEE ON LEGISLATION

The following items are quoted from *Bulletin No 21*, issued on October 27, 1945, by the Council on Medical Service and Public Relations of the American Medical Association.

HUMPHREY L. MCCARTHY, *Chairman*

* * *

October 27, 1945

WAGNER-MURRAY-DINGELL BILL (S 1050)

The Senate bill is still with the Committee on Finance and the House bill is with the Committee on Ways and Means. Neither committee has manifested any intention of early consideration of the bills, but Senator Wagner says he expects to have hearings on his bill held in the near future.

NATIONAL RESEARCH FOUNDATION BILL (S 1297, S 1285 and S 1248)

The three Senate bills authorizing the creation and financial support by the federal government of a national research foundation are being considered by the subcommittee of the Committee on Military Affairs. Hearings have been held for the last two weeks, and it is reported they will extend over another week or ten days. Members of the subcommittee are Senators Kilgore (West Virginia), chairman, Thomas (Utah), Johnson (Colorado), Murray (Montana), Revercomb (West Virginia) and Wilson (Iowa).

Among those who have appeared before the subcommittee are representatives of the Army, Navy, Departments of Agriculture, Commerce and Interior, United States Public Health Service and Bureau of the Budget, presidents and representatives of colleges and universities and representatives of large industries conducting scientific departments. Dr. Fishbein represented our association. Dr. Vannevar Bush, whose report *Science: The endless frontier* formed a basis of the bill, was a witness. That the Government should stimulate research and assist with appropriations is unanimously agreed, but there is a difference of opinion concerning how the Government shall be related to the work. Some recommend that there be created by the President a board of prominent scientists who shall select a director but he shall not have the power of veto. Others recommend that the President appoint a director and a board, giving the director full authority. Still others suggest that there shall be two boards, a scientific board and an administrative board, and that the director should be over the administrative board. Difficulty in separating fundamental, basic or curiosity scientific research from applied scientific research complicates the problem of administration. The hearings, when printed, will form a very valuable report.

MATERNAL WELFARE (S 1318)

Senator Pepper has not returned from his trip abroad but is expected before the end of the month. He announces that hearings will be held on the bill some time this year. In the meantime he is inviting a group of key people to give him their opinions concerning the merits of the bill.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATHS

BROWN — Lester R. Brown, M.D., of Laconia, died November 1. He was in his seventy-second year.

Dr. Brown received his degree from the University of Vermont College of Medicine in 1899.

His widow and one son survive.

been so clearly outlined by their discoverers Sims began the experiments that led up to his final report as early as 1845, after having observed the incontinence of urine, the ulcerated vaginas and the excoriated external parts that were the frequent sequelae of prolonged labor and poor obstetric practices. Many women of keen sensibilities, as he remarks, were excluded from all social enjoyment and were not unwilling to die rather than to face the extreme mortification of what was then considered a hopelessly incurable disease. Before 1852, Sims had many failures because his suture material, usually silk, would not hold. Other surgeons of the time reported similar difficulties, although Hayward,^{2, 3} of Boston, had reported one successful operation as early as 1839 and two more in 1851. One patient, however, was operated on six times, and another five. About 1849, Sims substituted silver wire for silk and was repeatedly able to close the fistulas permanently. In the paper in which he reported his results may also be found descriptions of the Sims's speculum and a self-retaining catheter. Thus two instruments were added to surgery that proved of inestimable value. Indeed, the year 1852 may be considered as the beginning of modern gynecology.

Sims was only too well aware of the importance of his work. In an address before the New York Academy of Medicine in 1857, he⁴ exclaimed

Silver as a suture is the greatest surgical achievement of the nineteenth century. For my country I claim the honor of this imperishable discovery, and seize this auspicious occasion to place permanently upon the record a history of its origin and progress. Many of you already know that it was not the result of mere accident, but of long, laborious and persevering effort, based upon the immutable principles of science, and forming one of the most beautiful examples of inductive philosophy.

We can perhaps, after all these years, forgive Sims

for his bombastic language, for he richly deserves the credit of perfecting this operation and of making it clear to the medical profession that the procedure was only consistently successful with the use of the Sims's position, the Sims's speculum, the special needles and the in-lying catheter that he had devised and, finally, the silver sutures. The details of the operation and the instruments are all well described and illustrated in the original paper, a con-

tribution well worth reading by surgeons of today. It has long been accepted, moreover, that Sims introduced silver sutures and that credit should be given him for this innovation in surgery.

Recently a unique copy of his address in 1857 was found in the joint library of the Harvard Medical School and the Harvard School of Public Health. This pamphlet, as noted on

the cover, was sent by Dr. Nathan Bozeman, an early associate of Dr. Sims in Montgomery, Alabama, to Dr. George Hayward of the Massachusetts General Hospital. Hayward wrote, opposite the passage quoted above in which Sims claimed the honor for his country, "The silver suture was used in London in 1834 in vesicovaginal fistula with success and the case was published in the *Lancet*."

One finds the article referred to by Hayward in the November 29, 1834, issue of the *Lancet*. Mr. Montague Gosset, a surgeon of London, in a letter to the editor of the *Lancet*, outlined a case report under the title "Calculus in the Bladder Vesicovaginal Fistula. Advantages of the Gilt-Wire Suture." He had operated in January of that year on a woman, previously unsuccessfully treated by Sir Astley Cooper, who had suffered from a fistula for over eleven years. Three sutures were passed; one was removed at the end of nine days, the second, at the end of twelve days, and the third was allowed to remain until three weeks had expired. The opera-

MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to

George L. Schadt, *Chairman*
Postwar Loan Fund
8 Fenway
Boston 15, Massachusetts

NEED FOR IMPROVEMENT IN MEDICAL CARE

To the Editor The editorial resort in the August 30 issue of the *Journal to the Christian Science Monitor* as devil's advocate has its amusing and ironical aspects, but these may as well be ignored, in that the *Journal* is customarily so much more liberal and intelligent than the *Journal of the American Medical Association*. However, the question to be asked is whether the suggested method of making the science of medicine socially useful — which of course is all that socializing means — is good or bad. The decision whether this is socialized or state medicine gets us nowhere, that is mere playing with words. But examine the system on its merits and indicate in what respect it is good or bad. I refer you to my article "Good Health in War and Peace" in the August issue of *Medical Record*.

T SWANN HARDING

Granite Gables
Falls Church, Virginia

In the article to which Mr Harding refers, he calls attention to the need for improved medical facilities, particularly in rural areas, and implies that such legislation as that proposed by the Wagner-Murray-Dingell Bill might be a means of accomplishing this. Cannot the same result be more surely, although more slowly, obtained on a voluntary-insurance and state-health-department basis? — Ed

DEPRIVATION OF LICENSES

To the Editor At a meeting of the Board of Registration in Medicine held October 18 it was voted that the registration of Dr Ensang W Cheng, 18 Tyler Street, Boston, be suspended for three months because of gross misconduct in the practice of his profession as shown by his conviction in court on a charge of conspiracy to commit abortion.

H QUIMBY GALLUPE, M.D. Secretary
Board of Registration in MedicineState House
Boston

To the Editor At a meeting of the Board of Registration in Medicine held October 18, the Board voted to revoke the registration of Dr Samuel S Keiner, 1203 Beacon Street, Brookline, for not less than five years because of gross misconduct in the practice of his profession as shown by his treatment of a patient.

H QUIMBY GALLUPE, M.D., Secretary
Board of Registration in MedicineState House
Boston

BOOK REVIEW

A Textbook on Pathology of Labor, the Puerperium and the Newborn. By Charles O McCormick, M.D. 8°, cloth, 399 pp., with 191 illustrations, including 10 in color. St Louis: C V Mosby Company, 1944. \$7.50

As stated in the preface, this book had its origin in a series of the author's lectures to the senior medical students at Indiana University.

The chapters on the pathology of labor, which comprise about three quarters of the text, are concise and the material is presented graphically in tables and schemas whenever feasible, a method that should be helpful to the student in grasping this complicated part of obstetrics. Pelvimetry, the classification of pelves and labor in contracted pelves are given considerable space. There is a note of conservatism throughout the chapter on operative obstetrics. The obstetric operations are classified and clearly presented with the aid of schemas and well chosen illustrations. The chapter on cesarean section is especially well done and forceps operations and version and extraction receive due consideration.

The second part, consisting of 56 pages is devoted to the pathology of the puerperium. Puerperal infection is adequately covered, and the material on sulfonamide and penicillin therapy, adds to the completeness of the treatment. Puerperal hemorrhage, its prophylaxis and treatment, the puerperal diseases of the breasts and the less frequent anomalies

and complications of the puerperium are brought to the attention of the reader.

The third part consisting of 42 pages, discusses the pathology of the newborn under three headings — conditions related to delivery conditions of congenital origin and conditions peculiar to the newborn period. Intracranial hemorrhage is well illustrated.

In the appendix the various forms of obstetric analgesia are discussed, and paraldehyde, pentobarbital and hyoscine (scopolamine) and continuous caudal anesthesia are mentioned. It is evident from the text that the author favors rectal ether anesthesia by the modified Gwathmey method.

This book should prove of value to the medical student and to the general practitioner of medicine who practices obstetrics.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Anatomy as a Basis for Medical and Dental Practice. By Donald Mainland, M.B., Ch.B., D.Sc., FRSE, FRSC, professor of anatomy, Dalhousie University, Halifax, Nova Scotia. 8°, cloth, 863 pp., with 61 illustrations and 11 tables. New York: Paul B Hoeber, Incorporated, 1945. \$7.50.

Dr Mainland has written a new textbook on anatomy for medical and dental students in which he has endeavored to present a text stripped of nonessentials but including all the clinical aspects of importance in active practice. The work is divided into three parts: the first deals with aims and methods, the second, with general anatomy, and the third with regional anatomy. The book is well printed on good paper, with a good type, and is easy to read.

Endocrinology of Woman. By E C Hamblen, M.D., clinical professor of endocrinology and associate professor of obstetrics and gynecology, Duke University School of Medicine and chief of the Endocrine Division and endocrinologist, Duke Hospital, Durham, North Carolina. 4°, cloth, 571 pp., with 157 illustrations. Springfield, Illinois: Charles C Thomas, 1945. \$8.00.

Dr Hamblen has written this new treatise as a successor to his *Endocrine Gynecology*, published in 1939, it is based on the clinical experience of the five years that have elapsed since the publication of the first book. The work has been streamlined for the benefit of third-year and fourth-year medical students, young medical officers and busy physicians. The subject matter is divided into five parts. The first and second parts discuss the biologic aspects of the endocrine glands and their physiologic relation to the female, the third considers the clinical and laboratory methods used in the diagnosis of normal and abnormal endocrine function, the fourth takes up the known diseases of function of the various endocrine glands in women, and the fifth applies the facts and theories of endocrinology to functional disorders and diseases of women and to obstetrics. In addition to bibliographic footnotes throughout the text, lists of selected references are appended to each chapter. The last chapter lists and describes commercial endocrine preparations. The book is well done in the characteristic Thomas style and is recommended for all medical libraries.

Approved Laboratory Technique. Clinical pathological, bacteriological, mycological, virological, parasitological, serological, biochemical and histological. By John A Kolmer, M.D., Dr.P.H., Sc.D., LL.D., L.H.D., professor of medicine in the School of Medicine and the School of Dentistry, Temple University and director of the Research Institute of Cutaneous Medicine, and Fred Boerner, V.M.D., associate professor of clinical bacteriology, Graduate School of Medicine, and assistant professor of bacteriology, School of Medicine, University of Pennsylvania and bacteriologist, Graduate Hospital, Philadelphia. Fourth edition. 8°, cloth.

WALLACE — Ellen A. Wallace, M.D., of Concord, died November 1. She was in her ninety-third year.

Dr. Wallace received her degree from the Woman's Medical College of the New York Infirmary for Women and Children in 1885. She was instrumental in founding the New Hampshire Memorial Hospital in Concord and was president emerita of the trustees.

MISCELLANY

COMMITTEE ON GROWTH OF THE NATIONAL RESEARCH COUNCIL

The appointment of the Committee on Growth, with membership designed to be broadly representative of the fields concerned in cancer research, both basic and clinical, has recently been announced by the National Research Council of the National Academy of Sciences. The committee was created, within the Division of Medical Sciences of the Council as a result of action by the American Cancer Society designating the Academy as its scientific adviser for research.

The committee calls the attention of interested investigators to the general outline of endeavor that it proposes to foster and to the general principles by which it will be guided. The committee accepts the interpretation of its field of interest as including reliance on, contact with and support of research in the basic sciences bearing broadly on the whole phenomenon of growth.

The committee has adopted the following major principles by which, in so far as possible, it will be guided in its sponsorship of research and training programs: the desirability of long-term grants to projects of major importance, grants, where possible, of such magnitude to permit individual investigators to appoint associates for long-term training periods, the granting of fellowships to institutions for training of workers to acquire new techniques and wider experience, the maintenance of continuing individual contact with workers in the field, the provision, on a participating basis, for continuing economic security for professional workers, and a liberal attitude toward the investigator's work publications and reports. To assist it in the fulfillment of its advisory functions the committee, on its part, will make free use of either *ad hoc* or standing subcommittees in specific fields of interest. Furthermore it proposes to arrange conferences of competent groups for discussion of problems, for interchange of reports and so forth, to make surveys to analyze problems or to determine progress in areas of special interest pertaining to cancer, to evaluate, through study by subcommittees and by the main committee, basic and clinical research undertakings and submit recommendations for support to the American Cancer Society, and to initiate and plan broad or specific programs of basic and clinical research through activities of the subcommittees and main committee and secure the co-operative efforts of investigators in the general undertakings.

The committee has established a central office in the Washington headquarters of the Council where information on all phases of cancer research will be assembled and from which reports may be distributed to interested investigators.

Many members of the committee have participated intensively in the broad programs of research conducted under the pressure of war. It is both the hope and the sanguine expectation of the committee that the fruitful pattern of co-operative investigations so successfully established during the war years, can now be carried on, modified and tempered to existing needs, into the continuing war against disease.

Membership of the committee, as now constituted, includes the following: Dr. C. P. Rhoads, *chairman*, Dr. Florence R. Sabin, *secretary*, Dr. A. R. Dochez, Dr. A. Baird Hastings, Dr. Charles B. Huggins, Dr. Donald F. Jones, Dr. C. C. Little, Dr. Carl R. Moore, Dr. John J. Morton, Dr. James B. Murphy, Dr. Eugene P. Fendergrass, Dr. Howard C. Taylor, Jr., Dr. M. A. Tuve, and Dr. M. C. Winternitz.

NOTE

The Institute of Pastoral Care has recently announced that Reverend James H. Burns, of Princeton, Massachusetts, has been awarded a clinical fellowship in pastoral care to begin January 1, 1946. This is the first time such a fellowship has been offered by the Institute, and it will provide both teach-

ing and research opportunities in the field of ministering to individuals. Mr. Burns will study under the direction of Reverend Rollin J. Fairbanks, Protestant chaplain at the Massachusetts General Hospital and director of the Institute.

CORRESPONDENCE

"TURN BACK, O MAN, "

To the Editor: I wish to offer you my heartiest congratulations on the fine editorial in the October 4 issue of the *Journal*, entitled "Turn Back, O Man, ". It raises to a very high level the editorial leadership of your journal. The inspiring hymn of Bax has stirred me deeply ever since I first heard it sung back in the twenties. I have had for years a copy of it pasted in my diary. It would have been better, if like you, I had broadcast its sentiments.

There is one point that I think needs clarification. You ask "how far science can be trusted." It is not a question of how far science can be trusted, but how far man can be trusted with science. I am sure that neither Bax nor the writer of your editorial is advocating that man turn back from his search for truth. It is from the path of turpitude he must turn back if he is to save himself from destruction. How to do that. One who lived on earth two thousand years ago has shown him.

J. H. MEANS

Massachusetts General Hospital
Fruit Street
Boston 14

* * *

To the Editor: The editorial in the October 4 issue of the *Journal*, "Turn Back, O Man, " is one that should not go unnoticed. It is a masterpiece.

If that human touch that a physician has with his patient is taken away, it makes no difference what science discovers it will become as "a sounding brass or tinkling cymbal."

HAROLD N. MCKINNEY, M.D.

149 Warren Street
Roxbury 19, Massachusetts

NURSES AVAILABLE FOR DOCTORS' OFFICES

To the Editor: I should like to call attention to the fact that the Placement Service of the Central Directory for Nurses is listing an increasing number of nurses who are seeking positions in doctors' offices. Physicians desiring this type of assistant should apply to this office.

MARY E. G. BLISS, R.N., Registrar
Central Directory for Nurses

420 Boylston Street
Boston 16

ANALYSIS OF WAGNER-MURRAY-DINGELL BILL

To the Editor: I was interested to note that the Committee on Public Relations of the Massachusetts Medical Society is trying to stimulate the members of the Society to obtain some knowledge of the Wagner-Murray-Dingell Bill (Senate 1050).

I have read with interest the analysis of the bill by the Bureau of Legal Medicine and Legislation of the American Medical Association, which was sent as a reprint to the members of the Massachusetts Medical Society. This, of course, represents one point of view.

Another analysis and discussion of this bill has been prepared by the Committee of Physicians for the Improvement of Medical Care, Incorporated.

If the Committee on Public Relations is anxious to have the members of the Society obtain as much knowledge as possible in regard to the bill, it is my hope that the committee will suggest that this analysis of the bill also be distributed to the members of the Society.

CHANNING FROTHINGHAM

1153 Centre Street
Jamaica Plain 30, Massachusetts

The 1944 Year Book of Industrial and Orthopedic Surgery. Edited by Charles F. Painter, M.D., orthopedic surgeon, Massachusetts Women's Hospital and Beth Israel Hospital, Boston. 12° cloth, 452 pp., with 282 illustrations. Chicago: The Year Book Publishers, 1945. \$3.00.

Dr. Painter in his preface stresses the importance of conservatism in the use of newer operations in the field of orthopedic surgery and calls attention to the extent of the contribution of military surgeons during the past year. He has made an able selection of articles, which should prove interesting not alone to orthopedic surgeons but to all surgeons handling traumatic injuries. The title in so far as it relates to industrial surgery is rather misleading, since this section is almost entirely devoted to industrial medicine and industrial toxicology. Only 15 per cent of the text is devoted to this vast expanding field, which might well have a yearbook of its own.

The Neurologist's Point of View: Essays on psychiatric and other subjects. By I. S. Wechsler, M.D. 8° cloth, 251 pp. New York: L. B. Fischer, 1945. \$3.00.

In this small volume Dr. Wechsler has devoted considerable space to the problems of the Jew in relation to medicine, he discusses nervousness and the Jew, the psychology of anti-Semitism, Moses and monotheism, Maimonides the physician, and the Palestinian and Russian colonization. Of special interest is an essay on the prevention of mental diseases, as well as one giving a brief history of psychiatry.

The Midwest Pioneer: His ills, cures and doctors. By Madge E. Pickard and R. Carlyle Buley. 4° cloth, 359 pp., with frontispiece. Crawfordsville, Indiana: R. E. Banta, 1945. \$5.00.

In this semipopular book, the authors have endeavored to tell the story of pioneer medicine in the Midwest in a non-technical manner. The period covered is from the first settlement of midwestern communities until about 1850. Appended to the text is a valuable list of sources containing the material relating to early medicine in the United States. This text should serve as an essential reference book for all medical libraries and for all persons interested in medical history.

The Doctor's Job. By Carl Binger, M.D. 8° cloth, 243 pp. New York: W. W. Norton and Company, Incorporated, 1945. \$3.00.

The author of this popular book has tried to give an account of some of the changes that have taken place in medicine in the last two decades. Special chapters on the choice of a physician, medical fees and etiquette and the relation of doctor and patient are included in the text. Dr. Binger briefly discusses medicine and psychoanalysis, psychiatry and medicine, and psychosomatic medicine. The various aspects of illness are considered in chapters on the cure and control of disease, the prevention of illness, office practice in hospitals, specialties and specialists, and socialized medicine. There are chapters on the common diseases, such as stomach ulcers, allergic conditions, asthma, tuberculosis and high blood pressure. The text is written in a smooth, readable style, interspersed with anecdotes, and should prove interesting to lay persons, as well as physicians.

The Specificity of Serological Reactions. By Karl Landsteiner, M.D., member, Rockefeller Institute for Medical Research, New York City. With a chapter "Molecular Structure and Intermolecular Forces" by Linus Pauling. Revised edition. 8° cloth, 310 pp. Cambridge: Harvard University Press, 1945. \$5.00.

This authoritative monograph was first published in 1936, and this revision was textually completed prior to the death of Dr. Landsteiner in June, 1943. The book is an account of the experiments on antigens and serologic actions with simple compounds, and a discussion of the phenomena of serologic specificity and related topics, with emphasis chiefly on the chemical aspects of immunologic reactions. The comprehensive bibliographies appended to each chapter have been greatly expanded in this second edition to include every article that the author regarded as worth while in the field of immunology. A new chapter on molecular structure and intermolecular forces by Dr. Pauling has been added to this edition. This reference monograph is recommended for all medical and

biological libraries and to all persons interested in immunology.

Clinical Heart Disease. By Samuel A. Levine, M.D., assistant professor of medicine, Harvard Medical School, physician, Peter Bent Brigham Hospital, Boston, consultant cardiologist, Newton Hospital, and physician, New England Baptist Hospital, Boston. Third edition, revised and reset. 8° cloth, 462 pp., with 157 illustrations. Philadelphia: W. B. Saunders Company, 1945. \$6.00.

This third edition of a standard text, first published in 1936, has been thoroughly revised to bring it up to date. The book has not been changed in its general character, and it continues to be a simple discussion of the common problems of heart disease that emphasizes the viewpoint of the general practitioner. New material has been added, including scleroderma heart, rupture of the valves, the heart in Addison's disease, the surgical treatment of patent ductus arteriosus and the chemotherapy, including penicillin, of subacute bacterial endocarditis. Two major additions have been made to the text. Because of the increasing interest and importance of electrocardiography, especially the precordial lead, the treatment of this section has been elaborated. Many new electrocardiograms have been added, illustrating the accurate methods of diagnosis that are now available by means of precordial electrocardiography. Also because of the growing interest in heart sounds and murmurs and their registration a brief description of phonocardiography and a number of sound records have been inserted in the text, in order that the reader might have a clearer idea of the significance of certain auscultatory findings such as gallop rhythm, changing quality of heart sounds and various heart murmurs.

Bibliographie der Luftfahrtmedizin. Zweite Folge 1936-1940. By Ingeborg Schmidt. In *Luftfahrtmedizin* 8:1-128, 1945.

Aviation medicine is of outstanding importance at the present time, and this comprehensive bibliography will be welcomed by all persons interested in the subject. It should be in all medical libraries.

American Medical Practice in the Perspectives of a Century. By Bernhard J. Stern, Ph.D., lecturer in sociology, Columbia University, and visiting professor of sociology, Yale University. 8° cloth, 156 pp. New York: The Commonwealth Fund, 1945. \$1.50.

This book gives an account of the reciprocal interplay between social, technologic, and economic forces in medicine. Dr. Stern begins his story with a broad description of the industrial and social conditions that prevailed in the United States early in the nineteenth century. Against this background, he outlines the characteristics of the medical education and practice of the period. He then traces the evolution of the social and economic world of today, revealing the effects that the growth of machine production, industrial urbanization and economic concentration have had on the health of the people. Parallel to this development the author sketches the concurrent growth of medicine, the increasing costs of its services, the increasing duration and costliness of medical education, the growth of specialization, the development of the modern hospital and the extent of the present distribution of medical care. In various chapters are discussed the relation between the specialist and the general practitioner, the supply and distribution of physicians, the patient load in medical practice, the income of physicians and the distribution of medical services. An appendix considers the effect of recruitment on the supply of physicians in civilian areas. This monograph should prove valuable to all persons interested in medical economics and social medicine.

Medical Uses of Soap. A symposium. Edited by Morris Fishbein, M.D. 8° cloth, 182 pp., with 41 illustrations. Philadelphia: J. B. Lippincott Company, 1945. \$3.00.

In this symposium, a number of authorities write about the various medical aspects of soap. In order are discussed soap technology, the effects of soap on normal and diseased skin and on the hair, and soaps for industry, for the industrial worker and for shaving. Dr. Fishbein contributes a chapter on the medical uses of soap, and there is also a chapter on cutaneous detergents other than soap.

1017 pp., with 346 illustrations. New York: D. Appleton-Century Company, Incorporated, 1945. \$10.00

This new edition of an authoritative text has been thoroughly revised, largely rewritten and considerably enlarged by the inclusion of new methods and new illustrations. Sections have been added on methods of examination of the saliva, pancreas-function tests, examinations of the blood and urine for hormones and vitamins, and virological examinations. The sections on examinations of the feces, blood and tissues for parasites have been revised. The sections on mycological examination and on skin tests have been rewritten to bring them up to date. Many new tests and methods that have become thoroughly established have been included in the text. A new type and a new format have been used for this edition, which is well printed on good paper and is recommended for all medical libraries and all physicians who are interested in diagnosis.

Cinchona in Java. The story of quinine. By Norman Taylor. With an introduction by Pieter Honig. 8°, cloth, 87 pp., illustrated. New York: Greenberg, 1945. \$2.50

Mr. Taylor is director of the Cinchona Products Institute in New York. He has written an interesting popular account of the discovery of cinchona and its commercial development particularly in Java, where the bulk of quinine used by the world is produced.

The Story of a Country Medical College. A history of the clinical school of medicine and the Vermont Medical College, Woodstock, Vermont, 1827-1856. By Frederick C. Waite, A.M., Ph.D. 8°, cloth, 213 pp., with 8 illustrations and frontispiece. Montpelier: Vermont Historical Society, 1945. \$4.50

In this volume the author tells the story of an early New England medical school and also describes medical education during the period before 1827, giving a general explanation of the background and conditions that made country medical colleges a logical step in the education of the time. A valuable list of over 1400 students who matriculated at that time is appended to the text. The volume should prove of interest to all medical, public and historical libraries, as well as those interested in medical history.

Poet Physicians. An anthology of medical poetry written by physicians. Compiled by Mary Lou McDonough. 4°, cloth, 210 pp. Springfield, Illinois: Charles C. Thomas, 1945. \$5.00

The author has endeavored to bring together examples of the verse of poet-physicians of all times, from Lucretius (98-55 B.C.) and Wang Wei (699-759 A.D.) to John W. Thompson (1906-). The selections are predominately from American and English physicians, as only sixteen out of a total of one hundred and ten persons listed are from countries other than the United States and the British Empire. Of these sixteen persons, seven are from Mexico, six from France and Italy, two from China and Japan and one from Germany. The classical period is represented by Lucretius, a great Roman poet but not a physician. The medieval poets are notable by their absence. The great mass of German poet-physicians are represented by Schiller, educated as an army surgeon but famous as a dramatist and poet. Victor Robinson, of New York City, is attributed to Russia, although he left there in his infancy and was educated, lived and worked in the United States. Likewise, Thompson, of Mexico, was educated in Edinburgh and lived, worked and taught in California. It seems as though it would have been better to have limited the selections to English-speaking physicians, resulting in a better rounded-out collection of verse, typical of one class of physicians. The book is well printed on good paper, in a delightful format, is easy to read and should be interesting to all physicians with literary inclinations.

Internal Medicine. Its theory and practice. Edited by John H. Musser, M.D., professor of medicine, Tulane University of Louisiana School of Medicine, and senior visiting physician, Charity Hospital, New Orleans, Louisiana. Fourth edition. 8°, cloth, 1518 pp., with 70 illustrations. Philadelphia: Lea and Febiger, 1945. \$10.00

This co-operative standard work is designed as a ready reference source for the physician and a textbook for the medical student. The work has been thoroughly revised, and over one hundred more pages have been needed to incorporate new material into the text. Sections on treatment with sulfonamides, penicillin and thiouracil have been included. A certain amount of space is devoted to the problems of war medicine, notably in conjunction with protozoan and metazoan diseases and acute infectious diseases. The section on rickettsial diseases has been entirely rewritten. New articles on military neuropsychiatric disabilities, war neurology and altitude sickness have been included in the volume.

Arterial Hypertension. Its diagnosis and treatment. By Irving H. Page, M.D., and Arthur C. Corcoran, M.D., Research Division, Cleveland Clinic Foundation. 8°, cloth, 352 pp., with 13 illustrations. Chicago: The Year Book Publishers, Incorporated, 1945. \$3.75

This manual for the care of the patient with arterial hypertension is designed for physicians whose special interests do not lie exclusively in this field. The important methods of diagnosis and treatment are considered, and as much of their theoretical background is given as will make their application in practice intelligent. The patient is considered as a whole in terms of the physical and mental deviations from the normal or the ideal that commonly precede, are incidentally associated with or result from the presence of hypertension. Selective bibliographies are appended to each chapter.

The Embryology of Behavior. The beginnings of the human mind. By Arnold Gesell, M.D., Ph.D., Sc.D. In collaboration with Catherine S. Amatruda, M.D. 8°, cloth, 289 pp., with 78 illustrations, 44 plates and frontispiece. New York: Harper and Brothers, 1945. \$5.00

The objective of this volume is to demonstrate the continuity that extends from the embryo to the fetus, to the infant and to the child, and to indicate some of the conditions and the mechanisms that give unity and dynamic design to the cycle of behavior growth. At the end of the text, there is an atlas of forty pages, which delineates the various phases of fetal and maturing infancy. A short list of selected references is contained in an appendix.

Shoulder Lesions. By H. F. Moseley, M.A., D.M., M.Ch. (Oxon.), F.R.C.S. (Eng. and Can.), lecturer in surgery, McGill University, and assistant surgeon, Royal Victoria Hospital. 4°, cloth, 181 pp., with 70 illustrations. Springfield, Illinois: Charles C. Thomas, 1945. \$4.50

In this short treatise Dr. Moseley has endeavored to write for the busy medical man a short and up-to-date account of the present knowledge of diseases and injuries of the shoulder.

Medical Care and Health Services for Rural People. A study prepared as a result of a conference held at Chicago, Illinois, April 11-13, 1944. 8°, paper, 226 pp., with 12 charts. Chicago: Farm Foundation, 1944. Single copies, \$1.00, five or more copies, each 60 cents.

The Farm Foundation, through its experience in the field of rural medical care and health services, became convinced that the inadequate medical services and facilities in rural areas could only be relieved by the united efforts of the organizations and agencies concerned with the welfare of rural people. In line with this conviction, the Farm Foundation called a conference of a group of rural men and women, representing farm organizations in various sections of the country and of medical men and technical specialists, to consider the problem rural people face in obtaining medical care and health services. The conference was organized with a series of group meetings, and the subjects to be discussed were divided into four parts: the problems rural people face in obtaining medical care and health services, the essentials of a rural health service, plans and proposal for developing an integrated health service for all the people, and the development of a constructive program of medical and health services for rural America.

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THE NUTRITIONAL STATUS OF CIVILIANS RESCUED FROM JAPANESE PRISON CAMPS

ALLAN M. BUTLER, M.D.,[†] JULIAN M. RUFFIN, M.D.,[‡] MARION M. SNIFFEN,[§]
AND MARY E. WICKSON[§]

SEVERAL thousand United States citizens interned in Japanese prison camps in the Philippines from the latter part of December, 1941, to the middle of February, 1945, received diets that progressively became so inadequate as to result in marked nutritional deficiencies. The turmoil at the time of release and the exigencies pertaining between that time and embarkation for the United States prevented a systematic appraisal of the nutritional status of these persons during that period. The arrival of these citizens in West Coast ports, however, provided a momentary opportunity to make an appraisal not only of the deficiencies suffered from the inadequate diets consumed during imprisonment but also of the benefits obtained from the diets consumed during the approximately nine weeks following rescue.

One of us (A. M. B.) therefore submitted a memorandum to Dr. Lewis Weed, of the National Research Council, calling attention to the fleeting opportunity still existing for obtaining information from this group. The memorandum suggested the immediate dispatch of a team of three members to a port of arrival of these internees — an internist familiar with the clinical manifestations of nutritional deficiencies, a pediatrician interested in the effect of nutritional deficiencies on growth and development, including adolescent development, and a nutritionist experienced in obtaining by detailed dietary histories the data required for a relatively quantitative appraisal of the nutritional value of the diets ingested. It was further suggested that a survey conducted by such a team by means of examinations that could be accomplished within the momentary opportunity afforded during disembarking would provide a pilot study of what could be learned by such a team under limitations

of time and facilities. It was believed that the survey not only might yield information of nutritional value that would otherwise be lost but also, according to the adequacy or inadequacy of information obtained, might indicate the nature of the personnel and facilities suited to survey the immediate nutritional problems of many areas of Europe, India and Asia.

This proposal was immediately submitted to the Medical Director of the American Red Cross and the Surgeon General of the United States Public Health Service. Two days later the required personnel, without any equipment or prearranged facilities, was asked to report to the American Red Cross in a West Coast port within thirty-six hours.

A report of the information obtained by this team in three days of examining internees at a port of arrival is submitted herewith. For convenience the data presented in this report are divided into three parts — an analysis of diets, the nutritional status of adults, and the nutrition, growth and development of infants, children and adolescents.

ANALYSIS OF DIETS

Diets during Internment

The data in Tables 1-4 present information concerning rations received by internees at Santo Tomas, Hay-Holmes and Bilibid and at Los Banos. The figures in Table 1 represent the basic ration available according to the records of rations issued. The amounts received were probably somewhat greater, since the data do not include all food purchased at canteens, received through the package line or raised in gardens. Table 2 lists the actual food items of the diet in January, 1944, and thus presents a picture of the type of food consumed. Table 3 shows the average food value obtained per person from the relief packages received during internment. A supply of vitamin capsules (Multi-Cap)^{||} was received from the Red Cross in Decem-

^{||}The original content of the capsules was as follows: vitamin A 5,000 units, vitamin D 500 units, thiamine, 1 mg., riboflavin 2 mg. and ascorbic acid 30 mg.

*This study was made possible by the support of the American Red Cross at the request of the National Research Council and with the cooperation of the United States Public Health Service and the United States Army.

[†]Associate professor of pediatrics, Harvard Medical School, chief of the Children's Medical Service, Massachusetts General Hospital.

[‡]Associate professor of medicine and director of Medical Clinic, Duke University, Durham, North Carolina.

[§]Nutritionist, American Red Cross.

NOTICES

ANNOUNCEMENTS

Dr Charles H Allman, who has been released from duty in the United States Navy, announces the reopening of his office at 520 Commonwealth Avenue, Boston, for the practice of diseases of the ears, nose and throat

Dr Samuel H Boyer announces the reopening of his office for the practice of general medicine at 483 Beacon Street, Boston

Dr James Hawley Currens announces the opening of his office for the practice of internal medicine and cardiology at 1101 Beacon Street, Brookline

Dr Richard J Doyle announces the reopening of his office at 387 Essex Street, Salem, for the practice of obstetrics and gynecology

Dr Irvin George Gahm, who has returned from active service with the United States Army, announces the opening of his office at 344 Commonwealth Avenue, Boston

Dr David H Gersh announces the reopening of his office at 1194 Massachusetts Avenue, Arlington

Dr William M Shedden, who has returned from military service, announces the opening of offices at 270 Commonwealth Avenue, Boston, and the Co-operative Bank Building, Concord

Dr Dorathea Willgoose announces the removal of her office to 1175 Great Plain Avenue, Needham

Dr Lucile Williamson announces the removal of her office from 1101 Beacon Street, Brookline, to 412 Beacon Street, Boston

GRANTS FROM AMERICAN CANCER SOCIETY

The American Cancer Society, Incorporated, completed a successful campaign for funds last June. These monies were raised for three general purposes — research, education and service. A portion of this fund is to be administered by the Massachusetts Division of the society. Organized medical service or research agencies in Massachusetts are invited to make application to it for grants to support constructive projects. Funds this year are limited, but it is hoped that, through the information gained of needs, adequate funds may be forthcoming in future years.

Applications from Massachusetts institutions should be made to Massachusetts Division, American Cancer Society, Incorporated, 476 Boylston Street, Boston. Plans and budgets should be given in detail.

LEGISLATIVE CONFERENCE

A meeting to discuss bills relating to health matters will be held on Wednesday, December 12, at 10 a m, at the Gardner Auditorium, State House, under the joint auspices of the Massachusetts Department of Public Health and the Massachusetts Central Health Council. If necessary, the meeting will reconvene at 2 p m. Physicians, nurses and social workers interested in health promotion are invited to attend. The date of this meeting has been changed from December 13, as originally announced.

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY

The annual meeting of the New England Obstetrical and Gynecological Society will be held in Boston on Wednesday, December 12.

NEW ENGLAND DERMATOLOGICAL SOCIETY

The regular meeting of the New England Dermatological Society will be held in the Skin Out-Patient Department of the Boston City Hospital on Wednesday, December 12, at 1 30 p m. Colonel J E Ash, director, Army Institute of Pathology, will address the meeting at 4 30 p m. The topic will include the correlation of cutaneous and visceral lesions of various systemic diseases. A motion picture will be shown on the subject "New Guinea Lichen Planus."

NEW ENGLAND PEDIATRIC SOCIETY

A meeting of the New England Pediatric Society will be held on Wednesday, November 28, at the New Haven Hospital, New Haven, Connecticut.

PROGRAM

- 12 00 m Clinical Conference Dr Grover F Powers and staff James D Trask Memorial Room
- 1 00 p m Luncheon (price, 50 cents)
- 2 30 p m Presentation of clinical material Drs Bouvert, Darrow, Dunphy, Jackson, Walcher, Vaughan and Yannet Fitkin Amphitheater
- 6 00 p m Refreshments and dinner at the New Haven Medical Association, 364 Whitney Avenue, New Haven
- 7 30 p m Potentialities of Group Practice of Medicine Dr Franz Goldman, associate clinical professor of public health, Yale School of Medicine

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, NOVEMBER 29

FRIDAY, NOVEMBER 30

- *9 00-10 00 a m The Use of Human Serum Albumin in the Treatment of Edema of Renal and Hepatic Origin Dr George W Thorn Joseph H Pratt Diagnostic Hospital
- *9 00-10 00 a m Medical clinic Isolation Amphitheater Children's Hospital
- *10 00 a m-12 00 m Medical staff rounds Peter Bent Brigham Hospital
- 10 50 a m Ocular Manifestations of Cutaneous Diseases Dr Paul M Runge (Postgraduate clinic in dermatology and syphilology) Amphitheater, Dowling Building Boston City Hospital

MONDAY, DECEMBER 3

- *12 00 m-1 00 p m Clinicopathological conference Peter Bent Brigham Hospital

TUESDAY, DECEMBER 4

- *9 00-10 00 a m Medical clinic Infants' Hospital
- *12 15-1 15 p m Clinicorontogenological conference Peter Bent Brigham Hospital

WEDNESDAY, DECEMBER 5

- *12 00 m Clinicopathological conference Children's Hospital
- *12 00 m-1 00 p m Clinicopathological conference Cambridge Hospital

*Open to the medical profession

OCTOBER 1-DECEMBER 10 1945 and JANUARY 7-APRIL 22 1946 Metropolitan State Hospital Eleventh postgraduate seminar in neurology and psychiatry Page 314, issue of September 6

NOVEMBER 26 New England Heart Association Page 606 issue of November 15

NOVEMBER 28 New England Pediatric Society Notice above

NOVEMBER 28-30 and DECEMBER 1 American Association on Mental Deficiency Page 576 issue of November 8

DECEMBER 12 Legislative Conference Notice elsewhere on this page

DECEMBER 12 New England Dermatological Society Notice above

DECEMBER 12 New England Obstetrical and Gynecological Society Notice elsewhere on this page

DECEMBER 13 The Treatment of Venous Thrombosis Dr Robert R Linton Pentucket Association of Physicians 8 30 p m Haverhill

FEBRUARY 2 American Board of Obstetrics and Gynecology Page 514 issue of October 25

DISTRICT MEDICAL SOCIETIES

SUFFOLK
DECEMBER 6 Censors meeting

WORCESTER
DECEMBER 12 Worcester City Hospital
JANUARY 9 St Vincent Hospital
FEBRUARY 13 Worcester State Hospital
MARCH 13 Worcester Memorial Hospital
APRIL 10 Hahnemann Hospital
MAY 8 Annual meeting

pregnant or lactating women and hospital patients
Comments pertaining more specifically to the
diets at each camp follow

Santo Tomas During the first month of 1942 every one of
approximately 3500 persons lived on canned goods, fruit,
eggs and so forth sent in from the outside. The actual intake
was very low, the average per person per day being probably

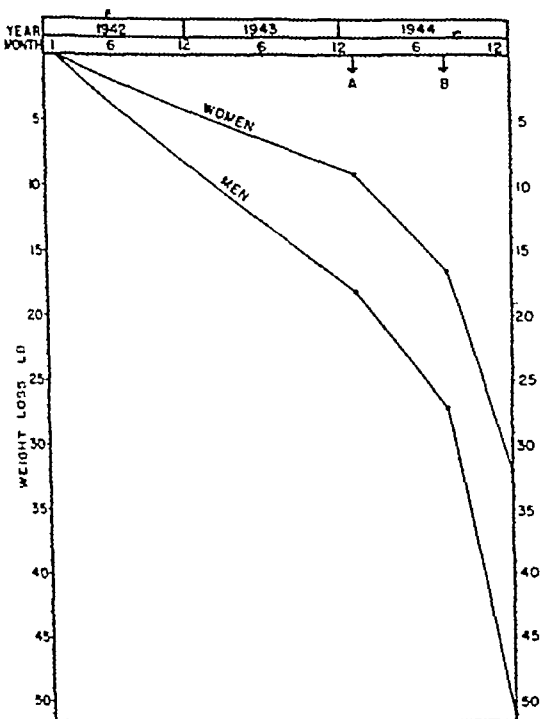


FIGURE 1 Average Weight Losses of Men and Women during Internment

A indicates when the package line closed (February 8, 1944), and
B the survey date (August 15, 1944)

less than 1200 calories. The people were in good shape, how-
ever, and hardly noticed the lack. A small loaf of rice bread,
a papaya and half a tin of milk per six persons, with an egg
and a cup of coffee apiece, was considered a good breakfast.
A tin of beans, bully beef, sardines or hash, a loaf of bread, a
little coffee, sugar and half a tin of milk composed the only
other daily meal for six persons.

Later those who had been in influential business positions
were able to arrange for food and the sending in of supplies.
Hundreds of Filipinos who were friends of internees denied
themselves to send food and delicacies to them. This food
was shared with those who had no friends. The Japanese

Two meals a day were served until July, 1942, for every one
except the kitchen staff, numbering 300, who had requested

TABLE 2 Comparison of Hospital Diet and Camp Diet at
Los Banos in January, 1944

Food	ALLOWANCE PER PERSON FOR MONTH	
	HOSPITAL kg	CAMP kg
Rice and flour	4.00	5.40
Bread	0.40	1.27
Cereal	1.60	—
Cassava	0.42	0.07
Sugar	0.70	0.70
Totals	7.12	7.44
Coconut milk	1.0	1.20
Camotes	5.0	4.30
Tomatoes	1.0	0.80
Condol	3.4	0.50
Squash	4.2	0.80
Red onions	0.3	0.14
Spring onions	—	0.02
Kinchay	0.1	—
Kangkong	—	0.40
String beans	0.1	0.1
Dried beans	—	1.46
Squidillas	0.3	—
Canned M and V Ration (80% vegetable)	—	0.44
Pechay	0.2	0.74
Totals	15.6	10.9
Cheese	0.17	—
Milk, condensed	0.11	—
Milk, dried	0.12	—
Totals	0.4	—
Carabao	3.50	2.15
Pork	—	0.50
Salmon	0.14	—
Dried fish	—	0.0
Pate	0.09	—
Ham and Eggs	0.05	—
Corned beef	—	0.15
Corned pork	0.04	—
Spam	0.07	—
Eggs, hen	0.10	0.02
Eggs, duck	0.40	0.05
Butter	0.16	—
Bouillon	0.10	—
Totals	4.65	2.88
Fat, vegetable origin	1.00	0.0
Margarine, vegetable origin	0.17	—
Totals	1.17	0.07
Bananas	0.70	1.0
Prunes	0.25	—
Totals	0.95	1.0
Tea	0.05	—
Coffee	0.25	0.16
Cocoa	0.11	—
Chocolate	0.04	—
Totals	0.45	0.16

three meals a day from the beginning because of heavy work.
After July, 1942, a noon meal was served to persons over
sixty years of age or those who had no money to buy food
for lunch.

TABLE 3 Total Content of Prisoner-of-War Food Parcels Received, together with Daily Average Amount
of Nutrients thus Provided per Person

FOOD PARCEL	TOTAL VALUE	PROTEIN	FAT	CARBO- HYDRATE	CALCIUM	IRON	VITAMIN A	THIAMINE	ASCORBIC ACID	VITAMIN D
	cal	gm	gm	gm	gm	mg	int. unit	mg	mg	int. unit
Canadian Red Cross relief kit ^a										
Amount per parcel	3282	0.71	123.0	460.0	7.2	104.0	28,880	3.0	48.0	3010
Daily average per person*	9	0.19	0.34	1.3	0.02	0.3	80	0.006	0.13	8
Far East American Red Cross package ^a										
Amount in 4 packages	51,544	1,984.0	3,080.0	32.0	0.8	117.284	29.72	2,608.0	—	—
Daily average per person*	141	5	8.4	0.1	0.8	321	0.08	7.0	—	—

*Most internees spread contents over 1 year, eating some once or twice a week

permitted buyers from camps to go out and purchase sup-
plies until February, 1944. Food was also obtained for cash
or credit at a package line, where bundles from outside were
received, and for cash only at the camp canteen.

On January 6, 1943, one Canadian Red Cross relief kit
(Table 3) and eight 8-ounce cans of corned beef were received
for each two persons. On December 15, 1943, each person
received four standard Far East American Red Cross pack-

ber, 1943 This was sufficient to provide an average of one capsule per day per person until October, 1944 The stability of these vitamin concentrates under the storage conditions that pertained and therefore the actual nutritional value are not known The small allowance of extra food† issued to those doing heavy work and to hospital patients is indicative of the critical shortage of food The actual total diet received by one woman during pregnancy is shown in Table 4

The quality of food brought into all camps by the Japanese was poor The greens received were

tables were not thrown into the pot until the last hours before serving

Probably not over 10 per cent of the internees at Santo Tomas and Los Banos suffered seriously from hunger during 1942 and 1943 Those who did so were either unable to adjust themselves to the strange foods or the conditions of internment or unable to digest the food because of illness The average weight loss per person during the first two years was approximately 13.5 pounds, as compared with a loss of 28.5 pounds, uncorrected for edema, during 1944 and a loss of 20 pounds, also

TABLE 1 Summary of Diets

DATE	TYPE OF RATION	TOTAL VALUE	PROTEIN	FAT	CARBO- HYDRATE	CALCIUM	PHOS- PHORUS	IRON	VITAMIN A	THIAMINE	ASCORBIC ACID	RIBO- FLAVIN
		cal	gm	gm	gm	gm	gm	mg	int units	mg	mg	mg
1/42-12/42	Basic	1900	68	45	300	0.3	1.0	23	4500	0.8	35	0.7
1/43-4/43	Basic	1900	65	50	300	0.3	1.0	20	3500	0.9	20	0.7
5/43-12/43	Basic	1500	55	30	250	0.2	—	—	3500	0.7	25	0.6
1/44-	Basic	1500	45	30	260	0.3	—	—	2400	0.7	20	0.3
2/44-6/44		1500	Variable but more restricted				—	—	—	—	—	—
7/44-12/44		1100	20	11	200	0.1	—	—	900	0.3	10	—
1/45-2/45		800	Still more restricted				—	—	—	—	—	—
	Extra ration for children and nursing or pregnant women	200	10	10	20	0.1	—	—	200	0.1	5	—
			Hay-Holmes (later Bilbid) Camp									
1/42-3/42	Temporary	400	—	—	—	—	—	—	—	—	—	—
3/42-7/44	Basic	1800	75	50	325	0.2	0.5	8	3000	0.6	25	—
8/44-12/44	Basic	900	20	10	190	0.1	0.4	6	700	0.1	10	—
1/45-2/45	Basic	700	15	10	150	None	None	None	None	None	10	—
			Los Banos Camp†									
5/43-12/43	Basic	2000	75	45	340	0.3	1.2	20	5600	0.8	30	0.7
6/43-12/43	Canteen	1500	30	55	200	0.2	—	—	2500	0.6	30	0.5
1/44-8/44	Basic	1800	45	40	315	0.2	0.6	11	4000	0.7	19	0.3
	Canteen	900	25	45	130	0.2	—	—	1000	0.4	19	0.4
9/44-2/45	Basic	1000	20	15	190	0.2	0.5	12	900	0.3	12	0.2
9/44-12/45	Canteen	150	3	15	5	None	—	—	100	0.1	2	None
Recommended allowances‡		3000	70	—	—	0.8	—	12	5000	2.0	75	1.0
Minimal requirements§		1850	50	—	—	0.4	—	9	1250	0.7	20	0.7

* Approximate daily average basic rations are estimated from amounts issued per person. Extra rations for children and nursing or pregnant women, as well as laborers were supplied by the camp. Values are based on estimated cooked portions of the food available and not what was actually edible. ‡

† Figures for average basic rations and canteen are not necessarily additive because of discarded distasteful food. ‡

§ As recommended by the Food and Nutrition Board, National Research Council.

¶ Averages of the minimal requirements given by the British Colonial Office and the United States Naval Medical Research Institute.

wilted and slimy, the rice was frequently dirty, the corn was moldy and had weevils, and the camotes‡ were often rotten. There was undoubtedly great loss in food value owing to the necessity of cooking in very large open vessels—*cawas*—and of using green wood as fuel. The sheer weight of the vessels required that cooks be chosen for strength rather than experience. The meat was always overdone. The vegetables for the first year and a half were cooked to shreds. The preparation of stew to be served at 5 p.m. was started at noon. Cereals were cooked for four or five hours. By the middle of 1943 there was improvement. Water in which vegetables were cooked was no longer wasted, meat added to the stew was precooked for three hours, and vege-

uncorrected, during the last six months of 1944 (Fig. 1). As shown by these weight curves, closing the camp and cutting off outside supplies in February, 1944, resulted in an acceleration of weight loss. That the rations were inadequate prior to August, 1944, is clearly shown by the findings of a medical survey on August 15, 1944,‡ which are summarized in Table 5. This, however, was but the beginning of dietary deficiency, as shown by the precipitous fall in weight (Fig. 1) in spite of the edema.

At Hay-Holmes, supplementation of the basic ration was difficult in the first few weeks and there was suffering from hunger during this period. After July, 1944, the food at all the camps became extremely inadequate, weight loss, weakness, edema, paresthesias and beriberi were experienced by most adults. Extra milk, cheese and tinned meat from Red Cross prisoner-of-war packets went to children,

† The following extra food was issued to certain persons daily at Los Banos in January, 1945: woodcutters, 200 gm.; gravediggers, 200 gm.; kitchen workers, 100 gm.; hospital staff, 100 gm.; hospital laundry workers, 100 gm.; and hospital patients, 250 gm. (rice), 125 gm. (lugao in place of corn or rice), and 200 gm. (camote).

‡ A vegetable resembling sweet potato.

when the average ration fell below 1900, and asked for food to be supplied in place of money. The Japanese promised the following daily ration from February, 1944, on

	g ^m
Rice or corn	400
Fruit and vegetables	200
Meat and fish	100
Sugar	20
Cooking oil	20
Salt	25
	765

This diet was approximated for only a couple of months and even then the meat promised was not provided. When camotes were furnished, 3 gm was considered by the Japanese equivalent to 1 gm of corn or rice, and this deduction was made from the corn or rice allowance.

Although the food had been inadequate from the beginning actual suffering from lack of food began to be general only in September, 1944.

Children under five years had one egg daily during the period April 7 to August 1, 1944. After August 1, children of twelve and under received 200 gm of vegetables four or five times a week, approximately 100 gm of which were camotes and 100 gm greens (mustard, talinum and pigweed). Additional requirements for children and hospital patients had to be taken from regular rations. Considering the small ratio of children to total population, the average reduction of general rations amounted to only about 5 gm daily.

The following statement issued by an administrative unit⁴ provides additional information concerning nutrition at this camp.

November 1, 1944 The general health of the camp has shown a sharp decline during the month of October. From the beginning of the camp in May, 1943, to September 30, 1944, only 12 cases of clinical beriberi had been diagnosed in the clinic. Seventy-seven new cases of beriberi were diagnosed during October, together with 113 new cases listed as avitaminosis and 162 as asthenia, both of which conditions are diseases of malnutrition and could be classified as incipient beriberi. In all, a total of 380 new cases attributable to malnutrition presented themselves at the camp clinic for treatment during the month¹. This brings the total of such cases that have been treated in the camp clinic to 1126, showing that more than 50 per cent of the camp has clinical signs of starvation.

The daily average caloric value of food served from the main kitchen has fallen during the month of October to the appalling figure of 881 [calories]. Reference to last month's hygiene and sanitation report will reveal that the writer pointed out at that time that the food being served in the camp was starvation rations. The October figures however have declined to 65 per cent of the 1345 calories issued daily in September. The epidemic of bacillary dysentery that has existed for the past two months seems definitely on the wane.

Diets after Liberation

After liberation internees subsisted for a short time on Army "hospital" and K rations. Noteworthy is the high incidence of diarrhea and exacerbation of edema that occurred at that time, which in many cases resulted in significant illness. During the voyage back to the United States the food aboard ship was adequate in calories and specific ingredients (Table 6). Craving for milk, ice cream and meat was general. Persons who had never been accustomed to drinking milk took it eagerly in addition to the regular food. Yet, in spite of this liberal dietary intake, several persons had a recurrence of edema in their feet during the voyage home.

NUTRITIONAL STATUS OF ADULTS

Ambulatory Internees

One hundred ambulatory internees selected at random from three ships were studied. In this way it was thought that a representative cross section could be obtained. Although a complete examina-

TABLE 6 *Average Daily Diet per Person Based on Amount of Food Checked Out of Ship's Stores During Twenty-Two-Day Voyage⁶*

FOOD ELEMENT	AMOUNT
Protein	116.0 gm
Fat	163.0 gm
Carbohydrates	311.0 gm
Calories	3164.0
Calcium	1.0 gm
Phosphorus	1.0 gm
Iron	24.0 mg
Vitamin A	8840.0 int. units
Thiamine	2.1 mg
Riboflavin	2.4 mg
Niacin	28.0 mg
Ascorbic acid	61.0 mg
Vitamin D	170.0 int. units

tion was not possible, a careful history was taken in every case and the eyes, tongue, gums, teeth and extremities were examined. The symptoms of deficiencies suffered by these persons during internment, as revealed by the history, the nutritional state at the time of arrival in the United States, and by such examination, are summarized in Table 7. We were impressed by the good state of health of most of these internees. They looked well, they were mentally alert, bright and cheerful, and, except for being underweight, they might not have been

TABLE 7 *Summary of Significant Facts Concerning 100 Ambulatory Internees*

DATA	
Symptoms of deficiencies during internment	63%
Edema	60%
Calf tenderness	54%
Paresthesia	43%
Diarrhea	36%
Sore tongue	36%
Poor vision	16%
Night blindness	11%
Sore gums	7%
Anorexia	7%
Nutritional state on return	
Good	78%
Fair	20%
Poor	2%
Edema still present	8%
Weight	
Average loss during internment	45 lb
Average gain on return	24 lb

distinguished from a corresponding group selected at random from any part of this country. Seventy-eight per cent of them reported that they felt well except for easy fatigability. It is of interest to note that pellagra was not found at the time of examination in a single case, there were no tongue changes and no cheilosis. No evidence of hyperkeratosis of the skin or of xerophthalmia or keratomalacia was observed. The gums were in remarkably good condition, as were the teeth, although most of the patients had cavities that required filling. Some tingling and an abnormal tendency of the hands and

feet to "go to sleep" were still noted by many of this group

Judging from the histories (Table 7), 63 per cent of this group had had edema while in camp. This was accompanied by paresthesia of the extremities. Tenderness of the calves was present in some cases, but usually no other pain. The edema varied from minimal pitting of the feet to a weeping edema of the feet and legs and a general anasarca involving the hands and even the face, although there was no history of ascites. Marked fatigability was described, but there was little to suggest congestive failure, although some internees noticed shortness of breath on exertion and some palpitation. There was no marked exertional dyspnea or cardiac asthma. Many of these persons complained of a marked polyuria and frequency of urination without dysuria or hematuria. This occasionally preceded the edema, although it was most marked while the edema was present and subsided after it had disappeared. It was impossible to determine with absolute certainty whether the edema was due to low plasma proteins or to so-called "wet" beriberi. A few of the internees had been able to obtain small amounts of thiamine. Some reported that their edema had been benefited by its use, others that it had not been effective. Polyuria and lessening of edema followed the intravenous administration of plasma in some cases. Diarrhea was frequent but was probably due to dysentery or some infectious agent. One of them gave a history suggestive of sprue. A history of sore tongue was frequent, but that of cheilosis was rare. Many had noted impairment of vision, which was probably related to a deficiency state. Sixteen per cent gave a history of night blindness. None gave a definite history of skin, conjunctival or scleral signs of vitamin A deficiency. Sore gums were noted in 11 per cent, but in none of these cases was there any particular tendency to bleeding. Susceptibility to ecchymosis from slight trauma was noticed by many. In general these findings by history are in close agreement with the observations of the medical survey in August (Table 5). The inadequacy of the diet prior to August, 1944, is apparent from the deficiencies manifest at that time. The gross inadequacy during the last five months is obvious from the accelerated weight loss (Fig 1), in spite of the previous depletion. It also accounts for the higher incidence of edema reported in the later histories.

Stretcher Cases

Twenty-five patients were stretcher cases and were taken immediately to the Marine Hospital in San Francisco. It was therefore possible to study them in much greater detail. The findings in this group are shown in Table 8 and are summarized in Table 9. In these patients, weight loss had been severe, the average loss being 55 pounds. Most

of them, however, were hospitalized not because of a deficiency state but because of some unrelated condition.

They gave essentially the same history as that obtained in the ambulatory group. On physical examination the most striking finding was the loss of

TABLE 9 Summary of Significant Findings Concerning 25 Hospitalized Returnees

DATA	
Symptoms of deficiencies during internment	
Edema	84%
Calf tenderness	84%
Paresthesia	84%
Diarrhea	60%
Sore tongue	44%
Dyspnea	25%
Anorexia	25%
Nausea and vomiting	20%
Physical examination on return	
Loss of vibratory sense	64%
Calf tenderness	40%
Poor vision	Several
Edema	4%
Weight	
Average loss during internment	55 lb
Average gain on return	23 lb

vibratory sense in 64 per cent of the cases. Calf tenderness was present in 40 per cent. Edema was found in only 1 patient. Knee jerks and ankle jerks were normal in all cases. The tongue showed nothing of significance, and there was no cheilosis. The gums were not spongy or bleeding. Nothing to suggest the dermatitis of pellagra was found. No vascularization of the cornea or Bitot spots were detected by slit-lamp examination, but a few of the patients were found to have a defect of vision apparently due to central scotomas. The skin showed no evidence of hyperkeratosis.

One patient had moderate pitting edema on admission to the hospital. This was not related to hypoproteinemia, since the total serum protein was 7.5 gm per 100 cc, the albumin being 5.5 gm, and the globulin 2.0 gm. The blood nonprotein nitrogen was 35 mg per 100 cc. There was no calf tenderness, but vibratory sense was absent over the feet. The heart by physical and x-ray examination was normal in size and position, and there was nothing to suggest congestive failure. The electrocardiograms were within normal limits. The patient unquestionably had a residual peripheral neuritis, as evidenced by the loss of vibratory sense.

Other Patients

Two hundred and fifty-two other patients returning from the Philippines had been admitted to the Marine Hospital before this study was initiated. Of the 24 admitted as ward patients, 7 had been classified as having a vitamin deficiency but had been discharged as recovered. The rest were treated for unrelated conditions. The remaining 228 patients had been treated in the Out-Patient Department. Of these, 49 had been classified as having malnutrition and a vitamin deficiency but had also been discharged from the clinic as well.

TABLE 8 Symptoms and Signs of Deficiencies as Revealed by History and Physical Examination of 25 Hospitalized Internees

AGE	SEX	SORE TONGUE	ANOREXIA	NAUSEA AND VOMITING	History			EDEMA	DYSPNEA	WEIGHT LOSS	WEIGHT GAIN SINCE RELEASE	Physical Examination				CALF TENDERNESSES	CLINICAL DIAGNOSIS
					DIARRHEA	PAROSYTHIA	LOSS				lb	WIGHT LOSS OF VIBRATORY SENSE	KNEE	ANKLE	JERK		
72	M	0	0	0	++	+	0	+++	0	103	?	++	+	0	0	0	Beriberi
66	M	0	-	0	0	++	0	++	0	62	20	++	+	+	+	0	Tuberculous (?)
49	F	+	0	0	0	++	0	+++	0	50	35	+	++	++	++	+	Rheumatic heart disease
52	F	+	0	0	+	+	0	++	0	50	20	+	++	++	++	+	Malnutrition
64	F	0	0	0	+	+	0	++	0	40	25	++	+	+	+	0	Heart disease (cause unknown)
50	F	++	+	0	+	+	0	+++	0	45	26	+	+	+	+	0	Hypertension
56	F	+	+	0	0	++	+	++	+	45	15	+	+	+	+	++	Hypertensive heart disease
65	F	++	+	+	+	+	0	++	0	57	16	+	+	+	+	+	Residual peripheral neuritis
62	F	0	0	0	+	+	+	++	+	26	25	0	+	+	+	+	Coronary disease
73	I	0	0	0	0	+	?	+	0	?	?	0	+	+	+	0	Pericious anemia
53	I	0	0	+	+	0	?	0	0	?	?	0	+	+	+	0	Arthritis
23	F	0	0	0	0	0	?	0	0	?	?	0	+	+	+	0	No disease
68	F	+	0	0	++	+	0	+++	0	50	35	+	+	+	+	++	Chronic colitis and neuritis
34	F	+	0	+	+	+	+	++	+	45	20	+	+	+	+	+	Fractured rib
52	F	+	0	0	0	+	0	++	0	70	37	+	+	+	+	0	Hemiplegia
80	F	0	0	0	0	0	?	0	0	?	?	0	+	+	+	0	No disease
52	F	+	+	0	++	+	0	++	0	60	15	+	+	+	+	+	Peripheral neuritis
28	F	0	0	+	0	+	+	++	+	46	22	0	+	+	+	0	Congestive failure (cause unknown)
60	F	0	0	0	++	+	+	+++	+	41	?	+	+	+	+	0	Cirrhosis
56	F	0	+	+	++	+	+	+++	+	60	15	+	+	+	+	0	Hypertension
70	M	++	++	0	+	+	0	++	0	60	?	++	+	-	+	+	Residual peripheral neuritis
37	M	+	0	0	++	+	-	++	0	82	40	+	+	+	+	+	Residual peripheral neuritis
35	M	0	0	0	++	+	0	+++	0	50	35	-	-	-	-	0	Peripheral neuritis
66	M	0	0	0	0	+	0	++	0	62	25	-	-	-	-	0	Periplegic neuritis
64	M	0	0	0	0	0	?	0	0	?	?	0	0	0	0	0	Pericious anemia

remained edematous until shortly before delivery on April 25. Much dental caries developed during pregnancy.

Mrs M was interned at Santo Tomas from January 6, 1942, to April 7, 1944, and at Los Banos from the latter date to February 25, 1945 (See basic diets for camps.) Supplements during pregnancy and the development of "wet" beriberi were the same as for Mrs H except that this patient received 5 mg of thiamine every 2 days during February, 1945. Edema cleared up 1 month before delivery on April 19.

Mrs McW was interned at Bacolod Camp from January 5, 1942 to March 10, 1943, at Santo Tomas from the latter date to April 7, 1944, and at Los Banos from the latter date to February 25, 1945 (See basic diets for camps.) She obtained supplements by purchase until October, 1944, and thereafter had some evaporated milk, eggs and vitamin capsules that she had saved. She also ate ground-up eggshells for their mineral content. She had no gross evidence of deficiencies during pregnancy.

Mrs McC was interned as was Mrs H. Menstruation was normal until pregnancy. Bacillary dysentery developed in September, 1944, and malaria in February, 1945. Beriberi developed during the latter part of pregnancy, with edema, calf tenderness, paresthesia, weakness and some palpitation. From July, 1944, to February, 1945, the reported diet was 150 gm of old and dirty polished rice daily, with moldy corn sometimes substituted, camotes twice a week with tops, weed tops, roots of trees and banana skins, rare banana, rare coconut, a total of eight cans of corned beef from October to November, 1944, a few beans, three calamansi a day until October and none thereafter, and one vitamin capsule a day to September, and two a day thereafter.

Mrs P was interned as was Mrs H. Dysentery occurred during the first 5 months of 1943 in December 1943 and in February, 1945. Amenorrhea developed in the 1st year of internment. There were nausea and vomiting during the first 2 months of pregnancy — May and June, 1944. The patient had beriberi with edema, calf tenderness, paresthesia and weakness during the last 3 months of pregnancy. The usual weight was 128 pounds. She lost 28 pounds during pregnancy, in spite of edema. On return to the United States, the weight was 120 pounds. She still had some peripheral neuritis and pain in the legs. From May to July, 1944, her daily diet was 300 gm of old and dirty polished rice, a small amount of sugar, camote and weed tops with small pieces of meat added to this stew twice a week, three bananas, a few beans twice weekly, occasional calamansi, a vitamin capsule and some extra amounts of vitamins A, B and C, and no milk, eggs or cheese. From August, 1944, to February 25, 1945, she had vitamins as mentioned, the rice ration was reduced to 200 gm daily, with moldy corn as a substitute. Spoiled fish was substituted for occasional meat. There were no bananas or fruit. From the 5th month of pregnancy the patient took daily two calcium tablets "of some kind" and she had a total of 4 pounds of powdered milk during the subsequent 5 months.

Mrs W was interned as was Mrs H. Her diet was the same as Mrs T's (Table 4). She had no milk during the last 3 months of pregnancy or during lactation.

Mrs T was interned as was Mrs H. Her diet is shown in Table 4. During internment she had amebic dysentery, nausea and vomiting, bleeding gums and, for the last 3 months while nursing, "wet" beriberi, with edema, weakness, calf tenderness, respiratory discomfort and paresthesia. She lost 25 pounds, but after her release gained 20 pounds.

Figures 2 and 3 give the heights and weights of the boys and girls over two years of age at the time of examination. Where the information was available the weights on release from internment and thus the weight gain during the nine weeks subsequent to that time are shown. The lines on the chart indicate the weights and heights per year of age below which 10, 25, 75 and 90 per cent of children fall on the basis of statistical average. The available evidence indicates that most of the children were underweight for their age at the time of rescue. The weight gain following rescue is impressive, particularly in the older children. The heights of the majority fall

below the 25-percentile line, many fall below the 10-percentile line. Under eight years of age this pertains equally to boys and girls. Above eight years of age the boys fall in a lower percentile group than

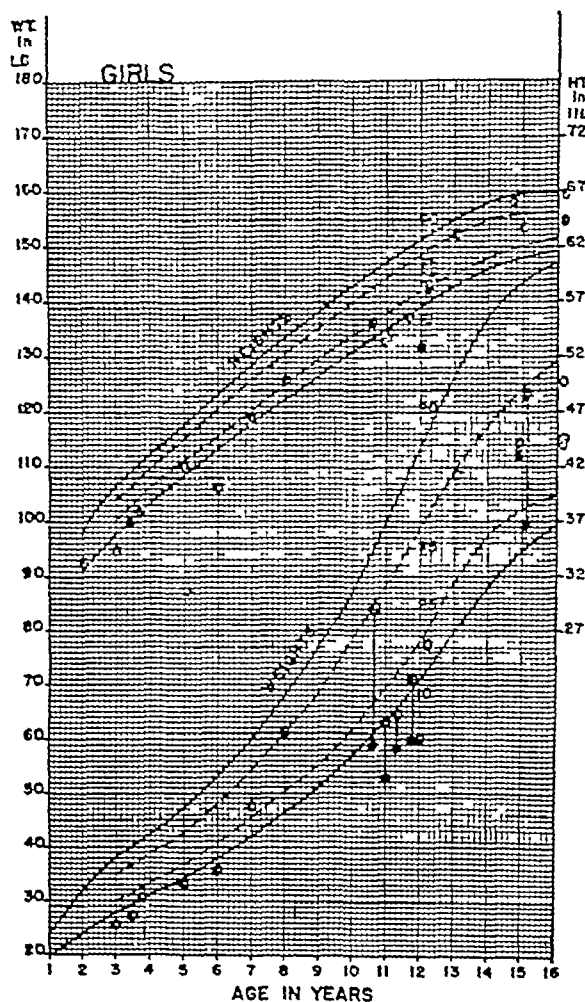


FIGURE 2 Heights and Weights of Girls
Where two dots are connected by a line, the lower dot is the weight on release from prison, and the upper dot the weight on arrival at a West Coast port. A single weight dot represents the weight on arrival.

do the girls. The data for boys and girls at the time of examination show that all the children were of fair weight for their respective heights. The greater retardation in height of older boys as compared with girls is clearly shown in Figures 4 and 5. Here the height age — that is, the age of the average normal child of the same sex and height as the subject — has been plotted against the actual age. Thus, the solid mid-diagonal line describes the average normal child. The broken lines correspond to the 10-percentile and 90-percentile lines of Figures 2 and 3 and thus establish the limits within which 80 per cent of normal children should fall. In a similar manner the weight age at the time of rescue and at examination is plotted on the figures. The data emphasize that

Later Findings

Additional information has subsequently been obtained concerning a few patients. Three other returnees who lived in Durham, North Carolina, were studied in detail at Duke Hospital. Their histories and physical findings were essentially the same as those noted above. Laboratory studies, including blood-cell counts, x-ray films of the chest, total serum protein concentrations and albumin-globulin ratios, plasma levels of vitamins A and C and carotene, electrocardiograms and urinary excretion tests of nicotinic acid, thiamine and riboflavin were all within normal limits.

Recent reports concerning some internees suggest that fatigue, neuritis, slight edema and dyspnea on

52 pounds at four weeks of age. The hemoglobin was 11.5 gm per 100 cc. Two others (L McC and W T) were under average length and weight for their age and had an architecture of the distal ends of the ulnar and radius, as described in the note to Table 10 that suggested the healing of previous rickets. Because these infants were exposed to sunlight, the ricketic disturbance may well have resulted from a deficiency suffered in the later part of fetal life. There was no craniotabes, ricketic beading, frontal bossing or other signs of rickets. A hemoglobin of 10.6 gm per 100 cc in one infant (W T) indicated a definite anemia.

In view of recent reports on the effect of diets during pregnancy on the development, growth and

TABLE 10 Data on Infants Born During Internment

NAME	SEX	BIRTH WEIGHT lb	AGE	HEIGHT* in	WEIGHT lb	PAST HISTORY AND DIET	CONDITION ON EXAMINATION
J H	M	—	2 wk.	20.5 (20.5)	8.2 (7.5)	Full term pregnancy, neonatal development normal (see mother's history during pregnancy), infant's diet adequate since birth	Healthy, hemoglobin 17 gm per 100 cc, x ray examination showed normal bones
R. M	M	—	4 wk	19.0 (21.0)	5.2 (8.5)	Full term pregnancy, neonatal development normal (see mother's history during pregnancy), infant's diet adequate since birth	Underdeveloped, pale, hemoglobin 11.5 gm per 100 cc, x ray examination showed normal bones but somewhat scanty subcutaneous tissue.
R McW	M	—	1 wk	20.0 (20.5)	8.2 (7.0)	Full term pregnancy, neonatal development normal (see mother's history during pregnancy), infant's diet adequate since birth	Healthy, hemoglobin 18 gm per 100 cc, x ray examination showed normal bones
L McC	F	6.5	2.7 mo	21.5 (23.0)	10.5 (11)	Full-term pregnancy, neonatal development normal, nursed 6 wk., then received adequate formula with supplements	Good condition, hemoglobin 12.4 per 100 cc, capitate and hamate bones not visible by x ray†
R F	F	6.5	2.9 mo	23.0 (23.5)	Fat	Full term pregnancy, neonatal development normal, nursed 1st wk., then received adequate formula with supplements	Good condition
A W	M	7.5	6.0 mo	24.0 (26.0)	Fat	Full term pregnancy, neonatal development normal, nursed for 3½ mo. to time of release, then received formula with adequate supplements	Good condition, no anemia
W T	M	6.0	6.0 mo	25.0 (26.0)	12.9 (17)	Cesarean section 2 wk. before term, neonatal development normal, nursing and formula as for A W	Moderately thin, hemoglobin 10.6 gm per 100 cc., bone age 3 mo
A C	F	8.0	24.0 mo	33.5 (33.5)	Average	Full term pregnancy, neonatal development normal, nursed 6 mo., then received low milk and protein diet and 1 vitamin capsule per day, occasional banana, 1 calamansi per week	Good condition, sat 8 mo., walked 13 mo., teeth good

*Figures in parentheses are averages for age.

†The distal ends of the ulnar and radius showed a cupping, lipping and increased density, which might best be interpreted as a previous rickets, with healing and dense mineralization of the previously uncalcified osteoid tissue.

exertion have persisted in a few cases for almost four months after liberation.

NUTRITION, GROWTH AND DEVELOPMENT OF INFANTS, CHILDREN AND ADOLESCENTS

This portion of the survey covers the dietary and clinical history and physical findings for 7 women throughout pregnancy, their 8 infants and 1 older infant, 23 children and 16 adolescents. Thus it provides data on the effect of the diets ingested by these pregnant women and children on nutrition, growth and development from fetal life to the maturation of the young adult.

Table 10 presents data on the height, weight, general condition and history of 8 infants born during internment. The effects of malnutrition were evidenced by only 3 of these infants. One infant (R. M.) was only 19 inches in length and weighed

health of the fetus and infant,¹⁰⁻¹⁴ the diet of one mother was analyzed as accurately as possible (Table 4). Although these mothers suffered similar internment, there was considerable variation in each case in the amount of supplemental food obtained by purchase. The data of Table 4 indicate the general nature of the diet of a person who benefited by such supplements as purchase could provide. Additional information specific to each case follows.

Mrs. H. was interned at Santo Tomas from January 5, 1942 to December 10, 1943, and at Los Baños from the latter date to February 25, 1945. (See basic diets for camps and Table 4.) During the first 2 months of pregnancy she obtained 4 ounces of evaporated milk daily and canned meat in small amounts twice weekly. Thereafter she received no milk and only a small cube of meat in stew every 2 or 3 weeks. During the 6th month she developed "wet" beriberi, with pitting edema of the legs extending above the knees, paresthesia of the hands and feet and weakness, because of which she was confined to bed from January to February, 1945. On liberation she was given thiamine daily and an adequate Army ration but

An x-ray film of the wrist of the ten-year-old boy weighing 70 pounds showed a bone age of 8.9 years, with normal density of bone and a normal muscle mass but not much subcutaneous fat on the forearm. His sisters of twelve, fifteen and eighteen years had grown and matured normally, although the older two were amenorrheic during the first and last months of internment (See S. R., K. R. and N. R., Table 12). X-ray films of the hand revealed bone ages corresponding to actual ages, with normal density of bone, good muscle mass and subcutaneous tissue. At the time of examination on arrival at the West Coast they had regained normal weights. These 4 persons are not included in Figures 4 and 5.

Tables 11 and 12 provide information concerning the adolescent development of these boys and girls.

cents revealed gross caries. In 2 the enamel was thin. On the whole the teeth appeared to be far better than those of children and adolescents observed in the outpatient clinics of Boston hospitals.

DISCUSSION

The high intellectual level of these internees and the fact that they suffered confinement where rations were carefully controlled and issued on a per capita basis made their records and observations more reliable than might pertain for many groups for which a nutritional survey is desired. Nevertheless, the analyses of dietary intake by such quantitative information as presented above have the limitation not only of considerable error but also of being only averages. Although the figures are

TABLE 11 Adolescent Development of Boys

NAME	ACTUAL AGE	SECONDARY PENIS*	SEXUAL TESTIS*	CHARACTERISTICS HAIR†		DEVELOP MENTAL AGE		MUSCLE LATENCY	POSTURE	COMMENT
				Pubic	Axillary	SEX	BOYS			
R. M. L.	14	+++	+++	++	0	14	1'	Good	Good	This half Philippine half American boy had lived normally in a Philippine home during the last 3 years. He was of average height and weight for his age and hence a good control standard.
D. F.	13	+	—	+	0	11	1'	Good	Good	Interned at Hays-Holmes 12/27/41-12/44 and at Bilibid 12/44-2/45 (See basic rations). Throughout 1944 received 1 vitamin capsule per day. He had 4 lb. of dried milk from 12/43 to 7/44 and no milk for the last 6 months. He grew but became thin and had weakness of extremities and calf tenderness.
T. R.	15	—	+	+	0	1	1'	Good	Good	Interned at Santo Tomas 1/42-2/45 (See basic rations). Milk and vitamin supplements as for D. R.
H. R.	17	++	—	++	0	14	1	Good	Good	Same as for brother T. R. He had also had jaundice for 2 wk. and intermittent diarrhea.
B. C.	19	++++	+++	+++	+	15		Good	Good	Interned at Santo Tomas 1/42-2/45. Milk and vitamin supplements as for D. R. He had had dysentery and measles during the last months; he had weakness, calf tenderness, edema and erectile impotence.

*Pubescent enlargement: + = questionable, ++ = slight, +++ = moderate, ++++ = considerable, +++++ = adult.

†Hair development: 0 = none, + = slight coarsening at base of penis only, ++ = extension laterally, +++ = extension upward.

Although the number of cases is meager, the data indicate that the early adolescent maturation of boys (see, D. R., T. R. and H. R.) together with their statural growth, was retarded. It may well be that the effect of the nutritional deficiency on the maturation of endocrine function was an important factor in the retarded statural growth. The girls clearly fared better. Although menstruation was somewhat irregular in some of them, which is not unusual in this age period, neither the menarche nor any other aspects of sexual development were delayed, nor was the bone age retarded. The greater effect of the inadequate nutrition on the development of adolescent boys as compared with that of girls appears to be further substantiated by observations on French school children made during the last years of the war.¹⁵

The teeth of only 1 of the 39 children and adoles-

maximal in the sense of representing amounts issued rather than consumed, they are not truly so because they do not include the extra supplements obtained on an individual basis by exceptional means. On the other hand, they are not minimal because they do not include deductions due to spoilage and lack of ingestion or digestion. They probably approach the mean consumed by most internees. In spite of the limitations, however, the dietary information accumulated in the short time and under the emergency circumstances of this survey has been in close agreement with such dietary records as were obtained later, and is indicative of the potential contributions of nutritionists trained in the technic of obtaining and analyzing careful dietary histories.

It is clear from the dietary data presented above, the average weight losses (Fig. 1) and the signs of deficiency revealed by the survey of August, 1944

these children were underweight for height when rescued, but had largely made up this deficit during the subsequent nine weeks.

The boy and smaller girl of three and a half years (Figs 2 and 3) were twins. They were born at term by normal delivery, the boy weighing 61 pounds and the girl 67 pounds. Neonatal and early development was normal. After internment at Santo Tomas in May, 1942, at approximately six months of age, they received restricted

was added at first two cans and later one can of meat per week, occasional extra rice and sugar, and coconut milk once or twice a month. During 1944 they

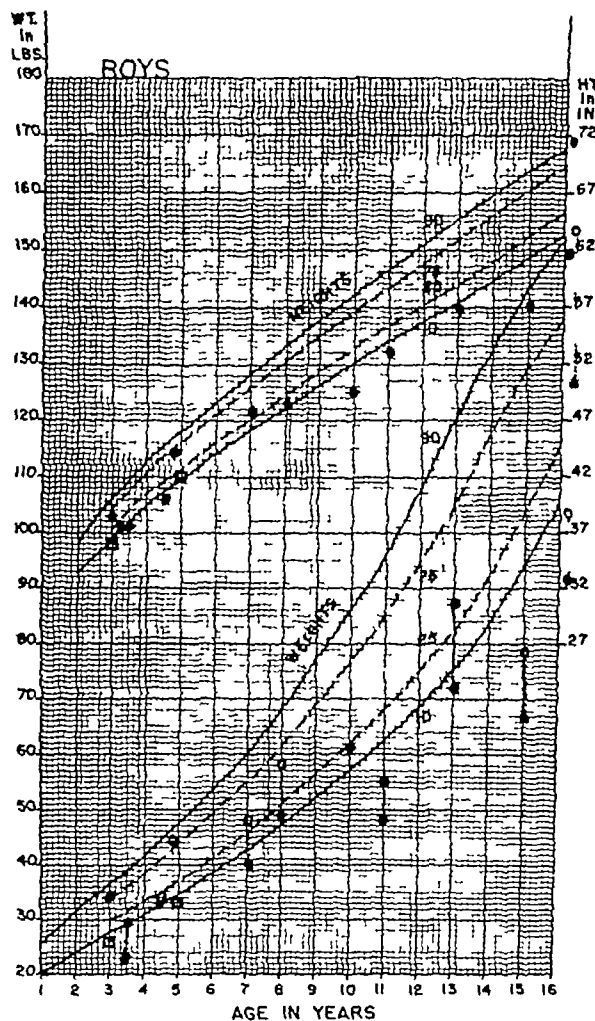


FIGURE 3 Heights and Weights of Boys

Where two dots are connected by a line, the lower dot is the weight on release from prison, and the upper dot the weight on arrival at West Coast port. A single weight dot represents the weight on arrival. The squares indicate children with paralysis due to poliomyelitis.

but fairly adequate diets, with the exception of milk, until two years of age, hence, the calcium was extremely low throughout. From February, 1944, to February, 1945, they received very little milk, the daily ration consisting of corn mush for breakfast, basic camp stew for lunch and bread sticks made of cassava flour and soy-bean soup for supper. To this

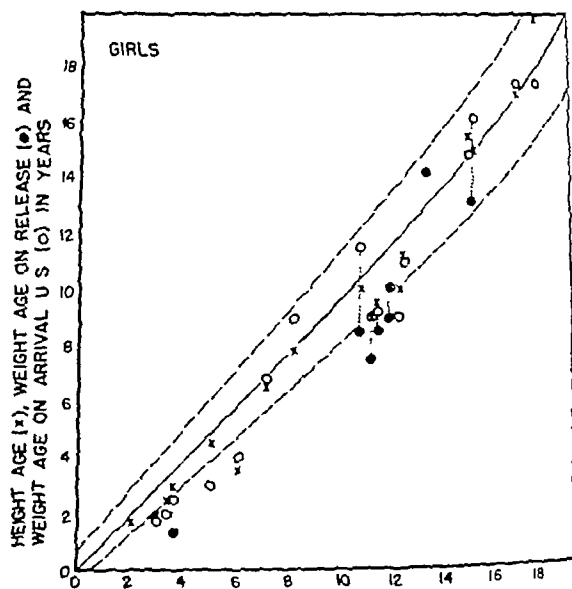


FIGURE 4 Comparison of Height Age, Weight Ages and Actual Age for Girls

received daily two vitamin capsules, 5 mg of thiamine and one "iron tablet." X-ray films of the hands and wrists on May 26, 1945, showed no lines

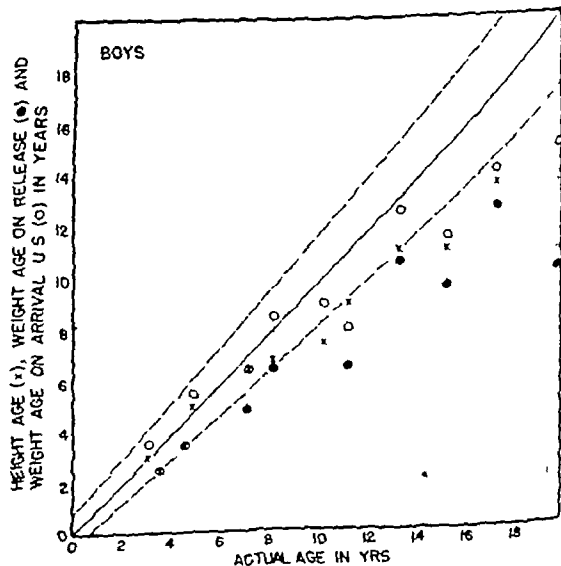


FIGURE 5 Comparison of Height Age, Weight Ages and Actual Age for Boys

of arrested growth. There was possibly some undercalcification of the metacarpal bones and phalanges. The bone age was 2.5 years, as compared with the actual age of 3.5 years according to Todd's standard.

due to vitamin A deficiency. The etiology of the central scotomas is uncertain. Similarly, the degree to which hypoproteinemia was a factor in the edema is uncertain. The nocturia appeared to be due to polyuria as well as frequency and was associated with polydipsia. The last may have been due to the fact that fluid was taken liberally to satisfy the feeling of emptiness and to offset the liberal salting of the food when salt was available. It is difficult to explain the massive weeping edema, with swelling of the feet, legs, hands, arms and face, on the basis of beriberi with congestive heart failure when so few patients gave a history of impressive shortness of breath on exertion, palpitation of the heart or nocturnal dyspnea. Although there is some evidence that thiamine resulted in amelioration of this edema, which was designated as "wet" beriberi, the factor of hypoproteinemia would be consistent with the low protein diet and the reported response to plasma infusions.

Because of the likelihood that both thiamine and protein deficiency occur under many conditions of dietary deficiency, provision for determination of the serum-protein concentration from a few drops of capillary blood should, if possible, be included in a nutritional survey, even under disaster conditions. In particular cases, hemoglobin determinations may also be informative. The error of this analysis, however, by any method that does not require considerable facilities is a distinct limitation. Other analyses of blood or serum provide evidence concerning deficiencies either so equivocal or merely confirmative or requiring facilities so difficult to obtain under disaster conditions that the desirability of making provision for them in emergency surveys seems questionable. Under the conditions usually pertaining in such surveys, the difficulty of collecting quantitative timed urine specimens in itself places a limitation on the quantitative significance of urine analyses.

An opportunity to examine these internees at the time of release would doubtless have permitted a more accurate definition of the maximal signs, symptoms and degree of deficiencies. The combination of history and examination at a later date has permitted, however, certain observations concerning not only the deficiencies suffered but also the degree of persistence or recovery resulting from nine weeks of normal dietary intake, and thus provides therapeutic and prognostic implications. These may be of particular value in appraising and meeting the problems of nutrition that present in many areas over the world today.

THERAPEUTIC AND PROGNOSTIC IMPLICATIONS

The rapidity of recovery of the majority of the adults from their signs of gross undernutrition and deficiencies is striking.

The most frequent residual of the deficiency state is peripheral neuritis. Many persons four months

after an adequate diet still have evidence of such neuritis. Several still complain of easy fatigability, dyspnea on exertion, slight edema and impairment of vision.

The gastrointestinal disturbances and exacerbation of edema incident to the abrupt shift from the inadequate diets to highly concentrated food suggest that the thiamine and protein intake should be increased gradually before patients suffering such deficiencies be permitted a high-calorie diet. It follows that the emergency food shipped to areas of malnutrition should be skimmed milk or other suitable proteins and vitamin concentrates rather than such highly refined carbohydrate foods as white flour and sugar. In the extremely weak person, properly administered parenteral glucose, amino acids and vitamins may be required before an adequate diet can be taken orally.

In view of the extremely restricted and inadequate nature of the diets ingested, the rapidity of recovery of these adults, the relatively good condition of the infants and the extent of the growth and maturation that occurred in the children justify a prognosis for such persons throughout disturbed areas of the world that is better than generally appreciated.

Appraisal of the beneficial effects of vitamin concentrates is difficult because of the role the protein depletion probably played in the edema. Moreover, the lability of the vitamins under the particular conditions of storage is not known.

It would be unfitting to omit a word of tribute to those with whom this report deals. Continually, while the information submitted here was being obtained, evidence of chivalry of men to women and of self-sacrifice of men and women for the sick or young was revealed that should be recorded in honor of these persons and as a tribute to the society whose code they adhered to under such trying circumstances. Rarely could one find a more intellectually eager, more co-operative, well-behaved or appreciative group of children than these youngsters at the end of their years of ordeal and the trying day of disembarkation.

We also record our admiration for the efficient and hospitable manner in which the American Red Cross and the San Francisco County Public Welfare Department provided for the many and varied needs of these returnees.

We also express our appreciation of the co-operation given us in conducting this survey to Major General C H Kells, A US, Colonel H N Villers, M C, A US, and Dr W Y Hollingsworth and Dr W Gordon, United States Public Health Service. We are indebted to Dr Harold Faber, Dr John Lyttle and Dr Milton Ream for the detailed examination of several children, to Mrs Vivian Harris, American Red Cross, for abstracting the records of the patients admitted to the Marine Hospital, to Dr Ruth Okey for advice in appraising the nutritional data, and to Dr T D Stevenson, Dr F O Smith and Major S M Bloom, M C, A US, for checking and supplementing the accuracy of our data.

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(Table 5), that the food intake during internment was below the maintenance standard from January 1, 1942, to February, 1944, and truly deficient from February to August, 1944. From then until release in February, 1945, the dietary data, the accelerated weight loss and the increase in the incidence of beriberi in most men who worked and in many women clearly prove that the food intake was grossly inadequate not only in calories but also in constituents. Certainly the diets ingested and the

festation of this specific deficiency when the diet provides less than 0.7 mg of thiamine per day (Table 1) agrees with findings under carefully controlled conditions.¹⁷ Niacin and riboflavin are not so heat labile. Because they occur in appreciable amounts in many foods, dietary deficiencies in these elements usually occur only on diets limited to a few specific ingredients. Moreover, the utilization of body tissue in starvation may provide an endogenous source that diminishes the dietary requirements of these

TABLE 12 Adolescent Development of Girls

NAME	ACTUAL AGE	Age of Onset	SECONDARY SEXUAL CHARACTERISTICS				POSTURE	DEVELOPMENTAL AGE		COMMENT
			MENSTRUATION	BREASTS*	HAIR†					
	yr		Regularity	Pubic	Axillary			SEX	BONE	
P C	11 6	0	0	+	0	0	Good	11		Internment and rations same as for boy D R. She had had malaria. She grew but became thin, and during the last months developed weakness and calf tenderness.
J R	12	0	0	+	0	0	Good	11	10	Internment and rations same as for brother D R. She had had a tonsillectomy and adenoidectomy and appendectomy. She grew but became thin and during the last months developed weakness and calf tenderness.
M C	12	0	0	+	+	+	Good	12		Internment and rations same as for boy B C. She had had measles. She grew but became thin.
S R	12	0	0	+	+	+	Good	12	13	Internment and rations same as for boy D R.
D C	13	12 5	0	++	++	++	Good	13		Internment and rations same as for sister M C. She had had enteritis and measles.
S G	15	13 5	Normal	++	++	++	Good	15		Internment and rations same as for boy D R. She had had bacillary dysentery twice. She had had some soreness of the tongue and during the last months developed weakness and calf tenderness. She grew 8 inches during internment.
E H	15	12	Normal	++	++	++	Good	15		Internment and rations same as for boy D R. During the last months she had "blackouts" on arising. She grew but became thin.
K R	15	?	Stopped first 2 and last 2 mo of internment	++	++	++	Good	15	13	Internment and rations same as for sister S R.
L G	17	Preinternment	Normal	+++	++	++	Good	17		Internment and rations same as for sister S G. She had had dysentery twice. During the last months she developed sore tongue, weakness and edema.
G R	18	Preinternment	Stopped first 6 mo then became regular	+++	++	++	Good	18		Internment and rations same as for brother T R. She ate extra rice and food allotted from diet of her father and mother. During the last months she developed edema.
N R	18	?	Stopped first 6 and last 8 mo of internment	+++	++	++	Good	18	18	Internment and rations same as for sister S R.

*Mammary development + = slight ++ = moderate +++ = full †Hair development 0 = none + = slight ++ = considerable

illnesses sustained during the first two years could have permitted but little storage of fat, protein, calcium or any of the vitamins other than vitamin D, which fortunately was abundantly provided by sunlight. During the last year there was, on the average, gross deficiency of many nutrients.

The predominant manifestation of thiamine deficiency as compared with other specific deficiencies is consistent with the low thiamine content of all food, the nature of the diet, its manner of preparation, the heat lability of thiamine and the short time required for such a deficiency to occur.^{16, 17} The mani-

festation of this specific deficiency when the diet provides less than 0.7 mg of thiamine per day (Table 1), and because these deficiencies take months to develop,¹⁸⁻²¹ absence of gross manifestation of vitamin A and C deficiencies is not surprising. The frequency of a history of night blindness, poor vision and ocular pain is particularly interesting because it has heretofore been reported so rarely. These symptoms appear to reflect neurogenic manifestations of thiamine deficiency rather than retinal dysfunction.

and incidence of valvular disease found on re-examination one to six months following discharge. Recheck examinations were made in 48 of the 65 salicylate-treated cases and in 25 of the 55 succinate-treated cases. In addition to physical examination

TABLE 2 Comparison of Therapeutic Effects of Salicylate and Succinate

FACTOR	TYPE OF THERAPY	
	TOTAL SALICYLATE (65 cases)	SUCCINATE AND ASCORBIC ACID (55 cases)
Period in hospital (days)	52	34
Period on drug therapy (days)	48	27
Incidence of drug toxicity (percentage)	19	2
Duration of fever (days)	11.5	5.7
Duration of leukocytosis (days)	22	14
Duration of accelerated sedimentation rate (days)	41	24
Incidence of carditis (percentage)	60	10
Incidence of relapse (percentage)	7	0

these comprised fluoroscopy (including esophagrams), teleroentgenographic measurement of heart size, electrocardiography and determination of the sedimentation rate.

The period of hospitalization averaged fifty-two days in the salicylate-treated group and thirty-four days in the succinate-treated group. The average duration of salicylate treatment was forty-eight days, and that of succinate treatment twenty-seven days. No toxic symptoms were observed in the cases receiving succinate except for flushing and slight mental confusion in a patient who received 80 gm daily. These symptoms promptly subsided on a reduction in dosage to 40 gm daily. Gastrointestinal symptoms, chiefly nausea, were observed in 10 of the 33 patients who received salicylate and sodium bicarbonate, whereas in the 32 salicylate-treated patients receiving 200 mg of ascorbic acid daily, nausea occurred in only 2 cases. One of these patients received 67 gm of salicylate daily and the other 53 gm daily.

The duration of arthritic symptoms, fever, leukocytosis and accelerated sedimentation rate was uniformly and significantly abbreviated in the succinate-treated group as compared with the salicylate-treated group. The white-cell counts and sedimentation rates were determined once weekly.

Findings that were considered indicative of carditis included murmurs, gallop rhythm, pericarditis, fluoroscopic or teleroentgenographic evidence of enlargement and electrocardiographic abnormalities. Signs of carditis developed in 69 per cent of the salicylate-treated cases, whereas they occurred in only 19 per cent of the succinate-treated cases. In computing the incidence of carditis, 4 cases in the salicylate-treated group and 3 in the succinate-treated group were excluded, owing to previous attacks of rheumatic fever with cardiac involvement that could not be attributed to the episode of rheumatic fever studied. Electrocardiographic abnormalities, chiefly prolongation of atrioventricular conduction, occurred in 55 per cent of

the salicylate-treated cases, compared with 9 per cent of the succinate-treated cases.

The incidence of relapses of rheumatic activity similarly was strikingly lowered in the succinate-treated cases. Seven relapses occurred after apparent subsidence of activity in the 65 salicylate-treated cases, whereas no relapses were observed in the succinate-treated group.

An attempt was made to determine the incidence of valvular disease by calling as many patients as possible back for re-examination following discharge from the hospital, after periods varying from one to six months. Forty-eight of the salicylate-treated cases and 25 of the succinate-treated cases were rechecked. In evaluating the occurrence of valvular disease, 3 salicylate-treated cases and 2 succinate-treated cases were excluded owing to cardiac involvement from previous attacks of rheumatic fever. Signs of valvular disease were present on re-examination in 30 (67 per cent) of 45 cases of the salicylate-treated group and in 7 (30 per cent) of 23 cases in the succinate-treated group. These figures do not represent the actual incidence of heart disease in the two groups, for many of those who fully recovered had returned to full activity and were not so readily available for re-examination as were the patients with residual signs of cardiac involvement, many of whom had prolonged convalescent care. In a series of 201 cases recently reported by Brown,⁹ it was found that 51 per cent of the patients had residual cardiac damage following acute rheumatic fever, with no significant variation in different age groups.*

Because of the striking difference in therapeutic response in the salicylate-treated and succinate-treated cases on all points analyzed, a further analysis was carried out in which only the severe cases of each group were compared. In these the temperature was at least 38°C, the white-cell count was at least 12,000, the sedimentation rate was over 60

TABLE 3 Comparison of Therapeutic Effect of Salicylate and Succinate in Severe Cases

FACTOR	TYPE OF THERAPY	
	SALICYLATE (27 cases)	SUCCINATE AND ASCORBIC ACID (28 cases)
Period in hospital (days)	69	47
Period on drug therapy (days)	64	38
Incidence of drug toxicity (percentage)	33	4
Duration of fever (days)	17	7
Duration of leukocytosis (days)	27	16
Duration of accelerated sedimentation rate (days)	58	35
Incidence of carditis (percentage)	65	21
Incidence of relapse (percentage)	3	0

mm per hour, and at least four joints were involved in the polyarthritides. The findings (Table 3) correspond closely to the observations on the entire series.

*In a study recently presented at the Eighteenth Graduate Fortnight of the New York Academy of Medicine it was reported by those connected with the Army Air Force Rheumatic Fever Control Program that 658 (64 per cent) of 1036 cases of acute rheumatic fever developed murmurs during the course of the disease.

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THERAPEUTIC MEASURES IN RHEUMATIC FEVER*

A Comparative Study of One Hundred and Fifty Cases

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BROOKLYN

IT IS not encouraging to reflect that the cause of rheumatic fever is unknown, that its symptoms are often obscure and its recognition is accordingly difficult, and that effective treatment is lacking. Still, much has been learned concerning this disease, and recent demonstrations of the effectiveness of sulfonamide prophylaxis constitute a notable advance in its control. Neither sulfonamides¹⁻³ nor penicillin^{4, 5} has proved of any value in the actual treatment of rheumatic fever.

The present report comprises an analysis of various therapeutic measures in 150 cases of acute rheumatic fever in young men treated during 1944. The types of therapy employed comprised the following: sodium salicylate (40 to 67 gm daily) and sodium bicarbonate (40 to 67 gm daily), 33 cases; sodium salicylate (40 to 67 gm daily) and ascorbic acid (200 mg daily), 32 cases; sodium bicarbonate alone (40 gm daily), 10 cases; sulfathiazole (6 gm daily), 15 cases; penicillin (50,000 units daily), 5 cases; and calcium double salt of benzoic acid and succinic acid benzyl ester§ (40 to 53 gm daily) and ascorbic acid (200 mg daily), 55 cases.

It was found, as others have reported, that neither sulfathiazole nor penicillin exerted any beneficial effect in the limited number of cases studied. Neither was sodium bicarbonate alone of any value. Because of the persistence and increased severity of symptoms, these types of therapy had to be terminated after a trial period of seven days.

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§Surgeon U S P H S (R).

§Supplied through the courtesy of the Seydel Chemical Company, Jersey City, New Jersey.

The two groups of salicylate-treated cases may be considered together, for with the exception of notable diminution of toxicity due to salicylate when ascorbic acid in place of sodium bicarbonate was given, no striking difference in therapeutic effect was noted. Others, such as Sendroy and Schultz,⁶ Schultz⁷ and Abt and his co-workers,⁸ have likewise failed to find any therapeutic benefit from ascorbic acid in rheumatic fever.

A comparison was made between the 65 salicylate-treated cases and the 55 cases treated with the succinate compound. The average daily dose of salicylate was 45 gm and that of succinate 42 gm. In all cases treatment was begun on the day of admission. The cases in these two groups were unselected, and were identical regarding age and clinical severity, as judged from the maximum sedimentation rate, the white-cell count, the temperature, the average number of joints involved in the polyarthritis and the degree of lowering of the plasma ascorbic acid level (Table 1).

The response to treatment was analyzed in the following categories (Table 2): period in hospital,

TABLE 1
Comparison of Salicylate-Treated and Succinate-Treated Cases

FACTOR	TYPE OF THERAPY	
	SALICYLATE	SUCCINATE
Average age	23 yr	23 yr
Highest temperature	38.5°C	38.7°C
Highest white-cell count	13,300	13,500
Highest sedimentation rate	76 mm per hr	78 mm per hr
Average number of joints involved	4.1	4.2
Lowest plasma ascorbic acid level	0.46 mg per 100 cc	0.43 mg per 100 cc

period on drug therapy, incidence of drug toxicity, duration of fever, duration of leukocytosis, duration of accelerated sedimentation rate, incidence of carditis, incidence of relapses of rheumatic activity.

apparatus for the synthesis of the dicarboxylic acids that "appear to play a fundamental role in the metabolic activity of many tissues" ²⁷ The concentration of succinic acid in muscle is 17 mg per 100 cc ⁴⁵ There is no evidence that a deficiency of the dicarboxylic acids exists in rheumatic fever, but numerous studies indicate a widespread interference with various enzyme systems involved in tissue oxidation

Porphyria was observed in rheumatic fever as long ago as 1880 by MacMunn ⁴⁶ More recently a careful study was carried out by Kapp and Coburn ⁴⁷ in 41 cases of acute rheumatic fever. A marked increase in porphyrin excretion accompanied or shortly followed the onset of rheumatic symptoms, but was not present during the preceding streptococcal pharyngitis or symptom-free interval before the attack. The intensity of porphyria was strikingly greater in severe than in milder rheumatic attacks. In pharyngitis alone and in other febrile diseases, such as influenza and pneumococcal pneumonia, the amount of urinary porphyrin was within normal limits in rheumatic patients, and in quiescent rheumatic patients in good health normal excretion of urinary porphyrins was found.

Ascorbic acid concentration has been found to be reduced in rheumatic fever by several investigators ⁴⁸⁻⁵⁰ In the present study, plasma ascorbic acid determinations were carried out in 120 of the 150 cases. Ascorbic acid levels were regularly reduced below the normal level (0.8 to 1.0 mg per 100 cc.), the degree of reduction paralleling the clinical severity. The lowering of ascorbic acid was unrelated to the previous nutritional status, since all the patients were known to have been on a fully adequate diet preceding their illness. Ascorbic acid has numerous functions in tissue metabolism. Although its role in hydrogen transport has not been clearly established, a relation to cellular oxidative processes is indicated by the demonstration that ascorbic deficiency in guinea pigs causes a marked drop in succinic dehydrogenase (cytochrome C reductase) activity in skeletal and cardiac muscle ⁵¹

Vitamin A is similarly reduced in rheumatic fever. Shank et al ⁵² observed that regardless of the concentration of vitamin A in the plasma prior to the onset of active exacerbations of the disease, there was a fall in the level of vitamin A in the plasma with development of acute rheumatic fever, the degree of decrease varying directly with the intensity of the rheumatic attack. Similar observations were made by Race, ⁵³ Ellison and Moore ⁵⁴ and Hall et al ⁵⁵ The role of vitamin A in tissue metabolism has not been entirely clarified, but Palmer ⁵⁶ has called attention to the unsaturated bonds acting as hydrogen acceptors. A relation of vitamin A to tissue respiration is suggested by the recent findings of greatly increased resistance to anoxia in rats fed with vitamin A ⁵⁷

Further indirect evidence of enzymatic inhibition in rheumatic fever stems from the reports of Massell and Jones, ¹ Swift et al ² and others, ³ as well as from our own experience, that sulfonamides exert a deleterious effect in this disease. Sulfonamides inactivate a variety of respiratory enzyme systems, particularly the dehydrogenases ⁵⁸ This inhibition is reversible by many substances, an extremely important group of which, according to Henry, ⁵⁸ comprises compounds related to cell oxidative metabolism — for example, coenzymes, glucose and carboxylic acids. Porphyria, a characteristic finding in rheumatic fever, as already mentioned, has been noted following the administration of sulfonamides ⁵⁹

Glutathione is not of itself a respiratory enzyme, but as stated by Barron ⁶⁰ it plays a role of fundamental importance in cellular respiration. It maintains the sulfhydryl group of a great variety of enzymes in the reduced —SH form essential for enzymatic activity. The total blood glutathione, almost entirely contained in the erythrocytes, is not characteristically altered in rheumatic fever, but it is significant that in fatal cases the oxidized fraction of glutathione is greatly increased ⁶¹ It is of interest that antirheumatic drugs — that is, colchicine ⁶² and salicylates ¹⁹ — increase the concentration of glutathione in the liver.

Vitamin A, ascorbic acid and glutathione are all reducing substances and are readily oxidized. They are physiologically active only in the reduced state, and the changes in these substances in rheumatic fever, as well as porphyria, suggest a widespread oxidative inactivation of tissue enzyme systems. Succinic acid is an extremely active reducing agent, and according to Harrow ⁶³ it is oxidized more rapidly than is any other substance known. It appears possible that in rheumatic fever administration of succinates not only helps to prevent inhibition of succinic dehydrogenase, thereby maintaining cytochrome in its reduced form, but may also prevent oxidation and inactivation of other respiratory enzyme system constituents.

Administration of ascorbic acid in conjunction with succinate appears to be indicated in view of the uniform finding of low plasma ascorbic acid levels in rheumatic fever and the observation that ascorbic acid deficiency causes a marked drop in succinic dehydrogenase activity ⁵¹ Administration of the calcium salt of succinic acid, as employed in the present study, likewise appears desirable, since calcium has a marked stimulatory effect on the activity of succinic dehydrogenase ^{42, 43}

SUMMARY AND CONCLUSIONS

A comparative therapeutic study was carried out in 150 cases of acute rheumatic fever. The types of therapy included the following: sodium salicylate and sodium bicarbonate (33 cases), sodium salicylate and ascorbic acid (32 cases), calcium

COMMENT

It is apparent from the data that the succinate compound was considerably more efficacious than salicylate in controlling the acute symptoms and signs of rheumatic activity, in shortening the duration of therapy and hospitalization and in decreasing the incidence of clinical relapses and signs of carditis.

Had larger doses of salicylate been employed, it is likely that they would have compared less unfavorably. Recently, Coburn¹⁰ has reported that in a series of rheumatic-fever cases receiving large doses of salicylate, varying from 10 to 12 gm daily, therapy was more effective than in another group receiving 3 to 6 gm daily, similar to the dose we employed. The hazard of toxicity with large doses of salicylate is not inconsiderable, for even with the relatively small dosage employed in this study, toxic symptoms occurred in 30 per cent of cases not receiving ascorbic acid. Sodium bicarbonate is relatively ineffective in decreasing the toxicity of salicylates, and any beneficial effect it may appear to have is deceptive in that in effect sodium bicarbonate depresses the blood level of salicylate, interfering with absorption and increasing renal excretion.¹¹

Ashworth and McKemie¹² have reported 2 cases in which death followed the giving of large doses of salicylate, as advocated by Coburn.¹⁰ Several investigators during the past year have reported other toxic effects due to salicylates,¹³ notably hypoprothrombinemia and bleeding tendency^{14, 15} and acidosis.^{16, 17} Salicylates, even in small doses, increase the urinary excretion of ascorbic acid.¹⁸ It has been reported that scurvy and death occur more rapidly in guinea pigs on a scorbutic diet receiving salicylate than they do in control animals on the same diet not receiving salicylate.¹⁸

Lutwak-Mann¹⁹ carried out an extensive study on the toxicity of salicylates, comparing them with cinchophen, sodium benzoate and other compounds. Her findings indicate a toxic effect on respiration of isolated liver slices, inhibition of formation of glucuronic acid synthesis by the liver and, in experiments on the whole animal, disappearance of liver glycogen. Further *in-vitro* studies demonstrated inhibition of a variety of isolated enzyme systems. In the whole animal, toxic effects on the nervous system, with death, and other findings, such as albuminuria, were regularly observed with large dosages. Cinchophen produced effects of similar magnitude, whereas in all the experiments benzoate in identical dosage was relatively innocuous.

These observations on benzoate are of interest, since benzoic acid is a constituent of the succinic compound employed in this study. Sodium benzoate was employed in rheumatic fever as long ago as 1878 by Senator,²⁰ who found daily doses of 8 to 12 gm to be harmless. Numerous studies by Gerlach,²¹ Chittenden,²² Herter,²² and Long²² have

established the lack of toxicity of the benzoates. As stated by Sollman,²³ the benzoates have a therapeutic action similar to but weaker than that of salicylates in rheumatic fever, and for this reason they have not been extensively employed. It is dubious whether the therapeutic effect noted in the present study with the calcium double salt of benzoic acid and succinic acid benzyl ester can be attributed in any appreciable degree to the benzoic acid component, since the total daily dose of benzoic acid was less than 2 gm. The succinic acid benzyl ester is readily hydrolyzed, releasing benzyl alcohol, a nontoxic compound with anesthetic and antispasmodic properties.²⁴ Benzyl alcohol is converted in the body to benzoic acid and excreted as hippuric acid.

Numerous studies during the last few years have demonstrated the important role of succinates and related dicarboxylic acids in biologic oxidation.²⁵⁻²⁷ Govier²⁸ has recently shown that sodium succinate protects to a great extent against the breakdown of coenzyme I in the cardiac muscle of dogs rendered ischemic by ligation of the coronary artery. Proger²⁹ demonstrated a stimulation of tissue uptake of oxygen in homogenized heart muscle by succinic acid, with an even greater catalytic effect under conditions of low oxygen tension. *In-vivo* experiments in dogs demonstrated a marked increase in arteriovenous oxygen difference following the intravenous administration of 1 gm of succinic acid, indicating greater tissue utilization of oxygen from the arterial blood. Proger further found that "anoxic effects on the heart muscle, as shown by the electrocardiographic examination, could often be prevented by the intravenous administration of succinic acid."

Succinic acid functions as a catalyst in the intermediary metabolism of carbohydrates³⁰ and fatty acids^{31, 32} through the Krebs citric acid cycle. A stimulating effect on cellular respiration on addition of succinates has been repeatedly observed.^{33, 35-37} Apart from its role as an intermediary in the Krebs citric acid cycle, succinic acid is intimately concerned in the oxidation reduction of cytochrome.³⁸ It reduces cytochrome, succinic dehydrogenase acting as cytochrome C reductase.³⁸ Succinates prevent the inactivation of succinic dehydrogenase by oxidized glutathione and a wide variety of inhibitors that react with the sulfhydryl group of the enzyme, converting the active reduced —SH to the inactive —S—S oxidized form.³⁹⁻⁴¹ Calcium has a marked stimulatory action on the activity of succinic oxidase.^{42, 43} Other biologic actions of succinates have been observed—for example, an increase in the synthesis of acetylcholine.⁴⁴ The various 4-carbon dicarboxylic acids, such as succinic acid, are supplied in part in the diet by citric, aspartic and glutamic acids but are synthesized chiefly in the liver by carboxylation of pyruvic acid.³⁷ Muscle tissue does not possess the enzymatic

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CORONARY-ARTERY DISEASE AMONG PHYSICIANS*

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IT IS well known by all physicians and even by the lay public that heart disease is at present the leading cause of death in this country. In fact, this has been so for some years. The great increase in the prevalence of this disease that has taken place during the last few decades has resulted mainly, if not entirely, from the increase in the number of cases of coronary-artery disease, hypertensive heart disease and other types of nonvalvular heart disease. There is no evidence that rheumatic valvular disease has been a factor in this change, and it is fairly clear that syphilitic heart disease has become less frequent. The most striking aspect of this question is the tremendous incidence of coronary-artery disease. The two obvious explanations that have been suggested are that angina pectoris and particularly coronary thrombosis are now much more readily and accurately diagnosed, and that the span of life has been so materially lengthened during the last fifty years that there now is a larger proportion of the population alive over forty years of age, an age period in which coronary disease is likeliest to occur. It is still uncertain whether coronary disease is more prevalent among the same age groups today than it was fifty years ago, despite the fact that many physicians have strong impressions that they are seeing younger and younger patients with coronary disease.

The incidence of coronary disease in relation to different occupations has also interested the medical profession, but the various views expressed have been conflicting. For the most part, the opinion prevails that professional men, such as physicians and lawyers, and business executives are more vulnerable to coronary disease than are laborers and farmers. The difficulty with most of the statistics

that bear on this question is that certain types of persons are more prone to seek advice from physicians, particularly consultants, than are others. When it is found that the proportion of physicians with coronary-artery disease going as patients to the Mayo Clinic is four times as great as that of laborers,¹ one can readily maintain that a physician with angina pectoris is likelier to go to a large clinic for an opinion than is a laborer. As a matter of fact, the statistics published by Master et al.² indicate little difference between the incidence of coronary disease among professional men and that among laborers.

It is obvious that the problem of the incidence of coronary-artery disease is difficult to unravel. There is one item of information that may indirectly throw light on the question that has not been sufficiently explored — that is, the age at death from coronary disease. It is reasonable to believe that if a particular group of persons is likelier to have coronary-artery disease than is the average population, the average age at death in that group will be less than the overall average age at death from coronary-artery disease. As illustrations of this principle one would expect patients with coronary-artery disease due to syphilis or occurring as a part of Buerger's disease to die at a younger age than those with only the customary coronary sclerosis. Heredity is accepted by all students as a significant etiologic factor in coronary disease. If one applies the above principle, it should be true that patients with angina pectoris who have long-lived parents will die at an older age than will those who have short-lived parents. It is interesting that such an analysis was made,³ and that it showed that in a group of cases of angina in which the average age at death of the parents was over seventy the average age at death was 63.4 years, whereas the corresponding figure for the patients whose parents lived to an average age of under sixty was 57.8 years. This difference of 5.6 years was significant and afforded indirect proof that heredity is a predisposing factor in the disease.

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double salt of benzoic acid and succinic acid benzyl ester (55 cases), sulfathiazole (15 cases), penicillin (5 cases), and sodium bicarbonate alone (10 cases)

Sulfathiazole, penicillin and sodium bicarbonate alone were without demonstrable therapeutic effect. No striking difference was evident in the two groups of cases receiving salicylate other than noteworthy diminution in toxicity in the patients receiving ascorbic acid in place of sodium bicarbonate.

Comparison was made between the 65 salicylate-treated cases and the 55 cases receiving the succinate compound. The average age and the severity of the disease in the two groups were identical, as judged by fever, leukocytosis, accelerated sedimentation rate, degree of polyarthritis and lowering of plasma ascorbic acid. It was found that on all points analyzed the cases receiving the succinate compound and ascorbic acid responded more favorably than did those receiving salicylate. The duration of acute symptoms, that is, fever, leukocytosis and accelerated sedimentation rate, and total days of hospitalization were uniformly and significantly abbreviated. Signs of carditis developed in 69 per cent of the salicylate-treated cases, compared with 19 per cent of the succinate-treated cases. Relapses of rheumatic activity occurred in 7 of the salicylate-treated cases, whereas no relapses developed in the succinate-treated cases. Drug toxicity was noted in 19 per cent of the salicylate-treated cases but in only 1 case (2 per cent) of the cases receiving the succinate compound.

Attention is called to the role of succinic acid as a catalyst in biologic oxidation. Evidence is cited that a widespread interference with various constituents involved in tissue oxidation occurs in rheumatic fever—that is, porphyrinuria, lowering of plasma ascorbic acid and vitamin A levels and changes in glutathione. It is suggested that there is an oxidative inactivation of various enzymes in this disease, and that administration of succinates may not only prevent inhibition of succinic dehydrogenase (cytochrome C reductase), but as an active reducing agent may also prevent inactivation of other respiratory enzymes. Calcium and ascorbic acid enhance the activity of succinic dehydrogenase, and the administration of ascorbic acid as well as the calcium salt of the succinic acid compound studied therefore appears to be indicated.

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ans and Gentile physicians has two possible explanations. Either Jewish physicians are more prone to coronary disease or the two age groups analyzed were not the same. If the latter were true, the average age at death of Jewish physicians dying from all causes should be considerably less than that of Gentile physicians. As mentioned above, the latter average was found to be 66.3 years. An analysis of the average age at death from all causes among 341 Jewish physicians who died during the years 1938 to 1942 was 57.2 years. It follows that the lower average age of Jews in the medical profession accounts for the fact that the age at death from coronary disease is so much lower among Jews than among Gentiles. It is interesting that the age at death from coronary-artery disease was only slightly less than at death from all causes in both groups.

The last comparison was made between smokers and non-smokers. These data were obtained from the private records of one of us (S. A. L.). The average age at death of 156 smokers was 58.2 years and that of 65 non-smokers 62.5 years. Although the numbers studied were not great, the difference of 4.3 years in the age at death seems significant. It cannot necessarily be inferred that smoking is the cause of this discrepancy, because smokers in general are younger than non-smokers, inasmuch as the consumption of tobacco has increased tremendously during the last two or three decades.

From the above study it appears that physicians die of coronary-artery disease at the same age as the average person with the disease. From this it can be inferred that the incidence of coronary-artery disease is no greater among physicians than it is among the general population. It was also found that Jews died at a younger age from coronary disease than did Gentiles, and smokers than non-smokers. This is probably due to the fact that the general average age of the two groups, Jews and smokers, that were studied was lower than that of the control groups, Gentiles and non-smokers.

SUMMARY

The age at death from coronary-artery disease was analyzed in various groups of people. It is believed that this affords indirect evidence of the influence that various factors may have in the development of coronary-artery disease, that is, if the age at death is distinctly lower in a group of a particular type, that factor must play an etiologic role in the development of the disease, provided the overall average age of the two groups is the same.

The average age at death from all causes of 2000 physicians was found to be 66.3 years. Similar figures for physicians dying of coronary-artery disease were 66.0 and 65.8 years for two different

series of cases (245 and 253 cases, respectively) occurring during the same year (1940). The latter figure is exactly the same as that found in patients with coronary-artery disease in the general population (65.8 years).

In general consultation practice the average age at death from coronary-artery disease among Jews was found to be 59.7 years and that among Gentiles 62.5 years in the experience of one consultant and 62.9 and 65.8 years, respectively, in that of another consultant. A similar but more striking difference was found in the deaths of Jewish physicians from coronary-artery disease as published in the *Journal of the American Medical Association* (56.7 years in 132 cases) as compared with that of Gentile physicians (65.7 years in 306 cases). This greater discrepancy (9.0 years), as compared with that among Jews in a general consultation practice (2.8 years), is ascribed to the fact that there were fewer Jewish physicians entering the practice of medicine forty to fifty years ago, and thus the average age of living Jewish physicians is lower than that of Gentile physicians. In support of this explanation is the finding that the average age at death from all causes among Jewish physicians was 57.2 years, in contrast to 66.3 years among Gentile physicians.

It was also found that the age at death was lower among smokers than among non-smokers — that is, 58.2 years in 156 smokers as contrasted with 62.5 years in 65 non-smokers.

The inference to be drawn is that the life of a physician is not conducive to coronary-artery disease and that the incidence of this disease among physicians is no greater than that in the general population, for both groups die at the same average age. Furthermore, although coronary-artery disease is the most frequent cause of death among physicians, it has no greater effect on longevity than does death from all other causes. Finally, the fact that Jewish physicians and smokers die of coronary disease at a considerably younger age than do Gentiles and non-smokers does not indicate any greater susceptibility of these two groups. It is a statistical consequence of the fact that the over-all average age of the first two groups is lower.

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The above method of reasoning was applied in the present study in three different ways. Physicians were studied by the above method in contrast to the general population, Jews in contrast to Gentiles, and smokers in contrast to non-smokers. If one of these groups were particularly prone to develop coronary disease, its average age at death would be lower than that of the comparative group.

The above reasoning seems to be valid when the over-all average age of any two groups that are to be compared is the same. The following illustrations help to clarify the point involved. The average age at death from coronary-artery disease in Army camps during the recent war was probably no higher than thirty to thirty-five years. This cannot be compared with the average age at death from coronary-artery disease in the general population, nor does it indicate that being in the Army is conducive to this disease. The reason is obvious: the age of the overwhelming majority of men in Army camps is only eighteen to thirty years. Likewise, the mortality statistics of physicians and other persons, Jews and Gentiles and smokers and non-smokers will be valid only if the average ages of the two types of population compared are essentially the same.

With this reservation in mind, and as a corollary of the above reasoning, if the average age at death from coronary disease is decidedly lower in a certain group, — for example, smokers as compared with non-smokers, — then that particular factor can be regarded as a material influence in the development of coronary disease.

A comparison was made between the average age at death from coronary-artery disease among physicians and that among the general population. For this purpose the statistics published in the *Journal of the American Medical Association* were analyzed. During part of 1940, the average age of physicians at death from all causes in 1000 consecutive cases was 66.3 years. Among these there were 245 who died of coronary-artery disease. Only the deaths with the following terminology were included in this group: coronary heart disease, coronary-artery disease, coronary thrombosis, coronary embolism, coronary sclerosis, coronary infarction, angina pectoris and myocardial infarction. The average age at death of this group was 66.0 years. As a control, another 1000 consecutive cases were analyzed from a different part of 1940. The over-all age at death was again 66.3 years. There were 253 deaths from coronary disease, and the average age at death was 65.8 years. It is of considerable interest that in a series of 445 cases of coronary-artery disease in a general consultation practice, reported by White et al.,⁴ the average age at death was 65.8 years. This figure happens to be identical with the one just mentioned for the average age at death of physicians. It follows that coronary-artery disease kills physicians at about the same average age as do all other causes, and that this age is the same as that

of other persons with coronary disease. Thus, the occupation of the physician is not conducive to the development of coronary heart disease, for if it were, the average age at death would be considerably lower than 65.8 years. The latter conclusion seems justifiable, because the average age of all physicians is essentially the same as that of all other persons who develop coronary heart disease. Inasmuch as physicians become practitioners at the age of twenty-six to twenty-eight, only the rare cases in which coronary-artery disease is fatal before that age would vitiate the above comparison. It is unlikely that this can introduce an error of more than 1 per cent.

An objection may be made to the above analysis because the physicians studied were almost exclusively men, whereas among the general population 25 to 30 per cent of coronary cases occur in women. In point of fact this tends to strengthen the above conclusion, for most women die from coronary-artery disease at an age at least two years older than men.⁵ It follows that the age at death of physicians from the disease would be about one year higher if there were the same proportion of women among physicians as is found in any group of persons with angina.

A similar analysis was made of Jews and Gentiles. The cases seen in consultation by one of us (S. A. L.) were analyzed for this purpose. It is fair to say that a consultant may be seeing a somewhat severer type of case than what occurs in the general population, so that the age at death may well be lower than the average. The same effect, however, would be produced on the data obtained concerning Jews as well as those concerning Gentiles. When 200 consecutive cases of coronary disease among Jews were studied, the average age at death was found to be 59.7 years, whereas that of 200 consecutive cases among Gentiles was 62.5 years. This difference of 2.8 years appears to be significant. A similar comparison can be made in the 445 cases of White and Miskall.⁶ The average age at death of the entire series was 65.8 years, whereas that of the Jews was 62.9 years.

Further support for this discrepancy was obtained when the average age at death of Jewish physicians was compared with that of Gentile physicians. Consecutive samples* of death notices in the *Journal of the American Medical Association* occurring during 1938 to 1942 were examined. The average age at death of 306 Gentile coronary cases was 65.7 years, practically identical with the previous figure of 65.8 years, whereas the age at death of 132 Jewish physicians was 56.7 years. This striking difference of 9.0 years between the two groups is much greater than that found in consultation practice (2.8 years).

The striking discrepancy between the ages at death from coronary disease among Jewish physi-

*It did not seem necessary to include all the coronary cases occurring during these years.

particularly the small and moderate-sized ones, which do not have a perforation of the omphalocele sac. Operation should be carried out promptly before the intestines become distended with swallowed air and before the omphalocele sac ruptures. Operation consists of excision of the sac and replacement of the omphalocele contents into the peritoneal cavity. The association of malrotation of the colon with this condition is frequent enough to warrant a routine search for the abnormality during repair of the omphalocele. In most cases the abdominal wall can be closed in layers, so that a firm abdominal wound is secured. In a few patients with a large omphalocele, however, it is practically impossible to close all the layers of the abdominal wall. Gross and Blodgett⁷ have pointed out that under such conditions it is only necessary to approximate the subcutaneous tissue and skin. At a later date the wound is reopened, and by that time the abdominal cavity has enlarged sufficiently to permit careful closure of the abdominal wall in layers.

The above authors have reported 22 cases, with an operative mortality of 50 per cent. Specht and Shryock⁸ report 5 cases, with 2 recoveries. O'Leary and Clymer⁹ review 91 cases in the literature and find a mortality of 21 per cent when operation is carried out under twelve hours. After twenty-four hours, the mortality increased to 61 per cent. These statistics are striking evidence of the need of early operation.

DIAPHRAGMATIC HERNIA

Until relatively recent years diaphragmatic hernia in the newborn was an almost completely neglected anomaly from a therapeutic standpoint. It is not too rare an anomaly, and without radical treatment the mortality approaches 80 or 90 per cent. Hedblom¹⁰ reports that 75 per cent of the patients with congenital diaphragmatic hernia die before the end of the first month of life. This includes hiatus hernias and, if these were excluded, the mortality would be considerably higher than the one he reports.

The diagnosis of diaphragmatic hernia in the newborn is not difficult. The infants present quite a typical appearance, characterized chiefly by attacks of cyanosis, particularly during or shortly following feedings. There is also a tendency to vomit. The respiratory rate is accelerated, owing to the encroachment on the chest cavity by the abdominal organs. Examination reveals the heart to be pushed to the opposite side from the hernia, with tympany to percussion in the region of the hernia, and auscultation often reveals a clear peristaltic sound. Because of vomiting and the danger of aspiration of barium, it is not warranted, except under unusual circumstances, to give barium by mouth. Almost invariably the diagnosis is clear in an x-ray film of the chest without the use of contrast mediums. The hernias are far more frequent on the left side than

on the right. These infants should be treated as emergencies, and operation should be delayed only until the fluid imbalance has been corrected. During the period of preparation, distention of the gastrointestinal tract is reduced by the use of Wangenstein suction and the administration of a high concentration of oxygen.

Harrington¹¹ reports 2 cases in which a transthoracic approach was utilized to repair the diaphragmatic hernia and in which, because of intra-abdominal adhesions, it was necessary to open the abdomen as well to reduce the hernia. The same author favors a transthoracic approach for hernias on the right side. Ladd and Gross¹² have reported the use of an abdominal approach and its advantages. Since the capacity of the peritoneal cavity is reduced in proportion to the volume of viscera in the chest cavity, closure of the wound may be quite difficult. Occasionally, the above authors found it necessary to close only the subcutaneous tissue and skin and to perform a secondary repair in seven or eight days. A careful closure of the layers of the abdominal wall is usually possible at the second operation.

Gratifying results have been achieved by operative repair of diaphragmatic hernia. Harrington¹¹ reported 21 cases in children, with 4 deaths. Ladd and Gross¹² reported the results in 16 patients who were operated on for congenital hernia. Nine of these recovered, 7 being under one year of age. Subsequently, at the Children's Hospital 25 patients with congenital diaphragmatic hernia have been operated on, with only 5 deaths — a mortality of 20 per cent, which shows an improvement of roughly 50 per cent over that of ten years ago.

INTESTINAL ATRESIA OR STENOSIS

Acute intestinal obstruction in the newborn is sometimes produced by atresia or stenosis of the intestines. Attention is directed to these patients by persistent vomiting of bile-stained material, starting soon after birth. The site of obstruction determines the amount of abdominal distention. Obstruction of the duodenum produces fullness in the upper abdomen, whereas atresia of the lower ileum results in marked general abdominal distention. Failure to detect cornified epithelial cells and bile in the meconium are important aids in making the diagnosis. Roentgenographic examination should be limited to plain films of the abdomen without the use of a contrast medium. From these the point of intestinal obstruction can be localized, since no gas is found beyond the atresia. It is dangerous to give barium because it is vomited and may lead to aspiration. Furthermore, it may form a concretion in the bowel, which becomes a hazard to the patient postoperatively after an anastomosis circumventing the atresia has been made.

It was formerly considered safe in infants with atresia to wait five or six days before operative in-

MEDICAL PROGRESS

SURGICAL EMERGENCIES OF THE ALIMENTARY TRACT OF THE NEWBORN

ORVAR SWENSON, M.D.,* AND WILLIAM E. LADD, M.D.†

BOSTON

IN THE newborn infant there occur not too infrequently congenital anomalies that, left untreated, result in death. Prompt recognition and adequate surgical correction of the anomaly will result in a gratifying low mortality rate. There are usually no serious associated congenital anomalies so that with correction of the major difficulty the child becomes normal. Not only is the mortality in a given case directly related to promptness of diagnosis and proper surgical treatment, but the period of recovery and convalescence in the hospital is decreased.

In the past there has been a well entrenched opinion among medical people that the newborn infant withstands surgical procedures poorly and that operations should be delayed on this ground whenever possible. Ladd¹ has pointed out that an infant during its first forty-eight hours of life presents a better surgical risk than it does a week or so later.

ESOPHAGEAL ATRESIA

One of the gravest congenital anomalies is esophageal atresia, with or without tracheoesophageal fistula. Yet the hopeless outlook of five or six years ago has changed considerably for the better. Freudenberger and Kerby² have reported no survivals without operation. The first successfully treated cases are now six years old.

This anomaly is more frequent than is usually considered to be the case. Ashley³ has collected 314 cases from the literature. The diagnosis is not difficult and is suggested in newborn infants by excessive mucus at birth and prompt regurgitation of even small feedings associated with attacks of cyanosis. Coarse rales in all parts of the lung fields with local signs of consolidation are usually present. Because of the frequently associated tracheoesophageal fistula, the abdomen is usually distended with air filling the stomach and intestines. The diagnosis is confirmed by passing a soft rubber catheter into the esophagus and finding an obstruction at about the level of the second or third dorsal vertebra. This procedure, as well as the injection of 1 or 2 cc of lipiodol through the catheter to outline the upper esophageal pouch, should be performed under fluoroscopic control. Such an examination demonstrates the level of the upper esophageal pouch and determines the presence or absence of a fistula connecting the upper esophagus and trachea. This

technic of radiographic diagnosis is far safer than the prevalent practice, in many institutions, of giving barium by mouth to outline the esophagus in infants. With the latter a portion of the regurgitated barium is almost invariably aspirated, which results in a severe and often fatal pneumonia.

Haight⁴ has reported 6 successful primary anastomoses of the esophagus in esophageal atresia out of a total of 24 patients operated on. Leven⁵ has reported 4 successful cases, in all of which multiple stage procedures were employed. Ladd⁶ has reported 34 cases with 11 survivals. To bring the experience at the Children's Hospital up to date, in the past six years there have been 64 cases, in 21 of which direct anastomoses were accomplished, with 5 survivals. In the remaining 43 cases, multiple-stage operations were performed. The latter consists of ligation of the fistula extrapleurally, followed by gastrostomy and marsupialization of the esophagus. At a later date an anterior thoracic esophagus is constructed, permitting the child to eat normally. In this group of 43 cases, there are 14 survivals. It is evident that the operation of choice, in cases in which the two esophageal segments are separated by more than 1.5 cm, is a multiple-stage procedure. If a primary anastomosis were attempted in all cases of congenital esophageal atresia, the mortality would probably exceed 80 per cent.

The chief cause of death has been pulmonary infection. Poor surgical judgment in selecting the safest plan of surgical treatment and associated congenital anomalies have also been factors in the still high mortality. Prompt recognition and surgical correction of this condition should bring a considerable improvement in the results.

OMPHALOCELE

This anomaly is such a striking abnormality in the newborn that it usually receives prompt attention. The condition consists of a herniation of abdominal contents into an abnormal sac-like umbilical cord, which consists of a translucent membrane composed of peritoneum and amniotic membrane. In rare cases the infant may be born with an omphalocele in which the sac is absent. The delivery, however, is usually without difficulty and the sac remains intact. If the infant does not receive prompt attention, the intestines become distended with enlargement of the contents of the omphalocele. As the sac is quite fragile, it may easily be ruptured, with evisceration of the abdominal contents. In most cases the anomaly is amenable to surgery,

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ectal pouch. Provided that the rectal pouch is less than 2 cm from the perineal skin and that there is no evidence of rectovesical or rectourethral fistula, anoplasty is indicated. Sigmoidostomy is imperative if the pouch is more than 2 cm from the perineum or if a fistula to the urinary system is present. In these latter cases it is possible to tie off the fistula and perform an anoplasty when the child is two or three years old. The presence of an adequate rectovaginal or rectoperineal fistula permits the postponement of anoplasty for two or three weeks if the child is not in good condition. It should be stressed that in long time follow-up, the usual rule is good sphincter control. Ladd and Gross¹⁹ stress the fact that anoplasty should not be delayed in uncomplicated cases beyond the first few days of life.

In newborn infants with anomalies of the gastrointestinal tract, Cohen²⁰ has pointed out that plain x-ray films of the chest and abdomen will, in most cases, give sufficient information for a definite diagnosis. Neuhauser²¹ has stated that, when barium is used in an infant who is vomiting, the danger of aspiration is a serious one, and that the pneumonia resulting from barium in the pulmonary tree is severe. This is particularly true in esophageal atresia and in all types of intestinal obstruction. Lipiodol outlines the esophageal pouch in patients with esophageal atresia as clearly as barium and is far less dangerous. On rare occasions, in cases of diaphragmatic hernia, it may be necessary to give a small amount of thin barium to verify the diagnosis. The tendency, on the basis of experience with adults, to give barium by mouth to sick infants is widespread. Consideration of the danger of this procedure and the realization that prac-

tically as much information can be secured from plain x-ray film without the use of a contrast medium make it clear that barium should be reserved for rare conditions in dealing with infants.

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tervention. It is now known that perforation may take place as early as two days after birth. Operation should be delayed only long enough to institute Wangenstein suction for combating abdominal distention, to correct the fluid balance and to give plasma or a small blood transfusion. During this short period of preparation the patient should be kept in an oxygen tent with a high concentration of oxygen to supplement the Wangenstein suction in lessening the abdominal distention.

Adequate surgical exposure to permit careful examination of the whole intestinal tract is imperative so that multiple areas of atresia are not overlooked. Erb and Smith¹² have reported a single survival after resection of multiple lesions. In obstructions of the duodenum and proximal jejunum, the operation of choice is a side-to-side anastomosis. In duodenal atresia, Ladd¹⁴ has pointed out that it is far more satisfactory to carry out a duodenojejunosomy than a gastro-enterostomy, since the latter causes loss of appetite and failure to gain weight properly. He reports a series of 10 cases of duodenojejunosomy, with 6 recoveries. At the Children's Hospital, since the above paper was published, there have been 3 additional cases of atresia of the duodenum, with 2 recoveries, and 8 cases of stenosis of the duodenum, with 5 recoveries. The lower the obstruction occurs in the small bowel, the less satisfactory are the results. Several years ago Mikulicz resections were performed for low ileal atresia, and the fluid loss from the ileostomy was frequently disastrous. It is now generally agreed that a primary anastomosis is indicated. A gratifying number of reports of single successfully treated cases are now appearing in the literature.

MECONIUM ILEUS

In contrast to the improved results that can be reported in most of the surgical emergencies of the newborn, no progress has been made in dealing with meconium ileus. This disease, caused by pancreatic insufficiency, is still uniformly fatal. These newborn infants usually present a picture of advanced intestinal obstruction. There is an early onset of vomiting after birth, the vomitus contains bile, and there is progressive distention. Neuhauser¹⁵ has pointed out that a diagnosis can be arrived at in about 40 per cent of the cases on the basis of plain films of the abdomen. Prompt exploration should be carried out. Because of Farber's studies¹⁶ on the effect of pancreatin on inspissated meconium, enterostomies have been performed on these infants, and an attempt has been made to clear the thick, tenacious meconium from the lower intestinal tract by using pancreatic enzymes as an irrigating fluid. In 4 cases the intestinal tract cleared. Pulmonary infection, however, eventually resulted in the death of these patients. Hurwitt and Arnheim¹⁷ have reviewed the literature and have been unable to find any cases of recovery.

MIDGUT VOLVULUS

A more hopeful type of intestinal obstruction, not too rare in newborn infants, is volvulus of the midgut. These patients with volvulus dependent on malrotation and faulty mesenteric attachment present the picture of an acute intestinal obstruction. In patients in whom a midgut volvulus is suspected, the diagnosis is confirmed by a plain x-ray film of the abdomen, which reveals a dilated duodenum and stomach, with only small amounts of gas in the intestine. It is important that operation be carried out promptly, since the volvulus obstructs the vascular supply to the bowel and neglect leads to infarction. Ladd¹⁴ has stressed the inadequacy of merely reducing the volvulus and the importance of freeing the malrotated cecum to relieve the duodenum of any obstructive bands, as well as the cecal mesenteric vessels. This is accomplished by freeing the cecum completely and placing it in the left upper quadrant, so that obstruction to the duodenum will not recur. The paper referred to above reports 23 cases of malrotation, with recovery in 19. There have been 7 additional cases in infants from the newborn group to the three-week-old group, with recoveries in all, making a total of 30 cases, with only 4 deaths. McIntosh and Donovan¹⁸ have reported similar good results.

IMPERFORATE ANUS

Imperforate anus is one of the most frequent surgical emergencies of the newborn and is usually promptly recognized. The complexity of the situation is frequently not appreciated, however, since the major anomaly is commonly associated with some type of fistula. Patients with rectovesical, rectourethral fistulas are the most difficult ones to treat. This is in contrast to the rectovaginal and rectoperineal fistulas, which carry the best prognosis, since the fistula presents an outlet for the intestinal tract. Infants with imperforate anus rapidly develop marked distention. It is of prime importance to determine how low the rectal pouch is in the pelvis to help determine the type of operation indicated. It is of equal importance to learn from the history and from observation whether the infant has passed or is passing gas and fecal material through the urethra with voiding or whether there has been or is a constant dribbling of small amounts of intestinal contents from the urethra. In the former situation, it can be deduced that the fistula from the rectal pouch connects with the bladder, whereas in the latter group of cases it connects with the urethra. Using Wangenstein's technic of inverting the baby and placing a metallic marker near the perineal dimple, it is possible to determine how near the pouch is to the perineum by taking a lateral x-ray film of the pelvis. This examination is only valid after fourteen to eighteen hours of life, since otherwise the gas may not have reached the

natically with a Banti syndrome and gradually developed increasing enlargement of the liver and spleen. Against this syndrome, however, is the fact that at no time did the patient show evidence of obstruction of veins of the stomach or esophagus and there was no vomiting of blood. Furthermore, against a Banti syndrome is the presence of nucleated red cells and immature blood cells in the peripheral blood.

I shall pause here a moment to ask the roentgenologist whether the bones were really coarsely trabeculated.

DR CLAYTON H. HALE: I do not believe that the trabeculation is any coarser than normal. They all stand out rather sharply, but it is a rather contrasty film.

DR JACOBSON: I think that this roentgenologic interpretation fairly well excludes one of the rare causes of a syndrome like this, namely, osteosclerotic anemia, a disease in which the bony overgrowth is tremendous and in which the large liver and spleen are often enlarged due to extramedullary hematopoiesis. Chronic nonleukemic myelosis can simulate this whole picture, but the absence of vomiting and of blood in the stools and the termination are against that disease.

I believe that the diagnosis boils down to either myeloid leukemia or some type of myelophthisic anemia, which is due to various causes.

By myelophthisic anemia I mean any new growth that infiltrates the bone marrow and interferes with normal maturation. This is a peculiar case if it is a case of myeloid leukemia, in view of the fact that the patient terminally developed only a slight anemia. Examination on only one occasion of several that we know showed a significant number of myelocytes or myeloblasts in the peripheral blood, and terminally the platelets were said to have been normal. Those are the three points against myeloid leukemia, but they do not rule it out. The only way to be sure during life is to study the morphology of the bone marrow.

In view of the patient's loss of weight, the fever, the night sweats, the general down-hill course and, finally, the evidence of small-bowel obstruction, one thinks of some type of neoplasm, intra-abdominal or retroperitoneal, which might have caused the whole picture. I rather think that that is the best bet. Would it account for the liver, the spleen and the blood picture? I think that it would. Abdominal carcinomatosis, or lymphoma, with metastases to the bone marrow can certainly produce this blood picture, which was leukemoid rather than leukemic. The large liver and spleen could have been due either to direct metastases or to myeloid metaplasia as part of the extramedullary hematopoiesis that was going on, or to both. Whether this was carcinoma, sarcoma or lymphoblastoma, I have no way of telling. So, I shall end with a diagnosis of abdominal car-

cinomatosis, with metastases to bone, a leukemoid blood picture and small-bowel obstruction.

DR KANE: This case was a puzzling one. From the onset the blood picture was confusing. Although the symptoms were only of three weeks' duration, because of the size of the liver and spleen I thought that the patient might have chronic myelogenous leukemia. The blood picture, although certainly not characteristic, was more in keeping with chronic rather than acute myelogenous leukemia. It had the appearance of a leukemia long treated by x-ray in which the white cells are depressed but the red cells remain young and nucleated. Four or five blood smears were examined, and all were essentially the same. It is interesting that the hemoglobin remained at about 70 per cent during his entire illness.

One week before entry he had an acute episode of nausea and vomiting, of which he had never complained previously. On admission he said that he had been constipated, and I thought that he had an obstructive lesion of the large rather than of the small bowel because he did not appear to be acutely ill. A barium enema was completely negative, and an abdominal flat plate showed only a little gas in the small bowel. Two days later a repeat flat plate showed tremendously dilated loops of small bowel and a Miller-Abbott tube was passed. Two days following this the picture began to become somewhat clearer and I thought that he might have had a mesenteric thrombosis on the venous side. He went into shock and died shortly thereafter.

DR JACOBSON: Do you think that at any time the peripheral blood picture was convincing for myelogenous leukemia?

DR KANE: I thought that, although not characteristic, it was not inconsistent with such a diagnosis.

CLINICAL DIAGNOSIS

Mesenteric venous thrombosis

DR JACOBSON'S DIAGNOSIS

Abdominal carcinomatosis, with bone metastasis, leukemoid blood picture and small-bowel obstruction

ANATOMICAL DIAGNOSES

Thrombosis of mesenteric veins

Gangrene of terminal ileum

Chronic myelogenous leukemia

Hemorrhage into adrenal glands

Bronchopneumonia

PATHOLOGICAL DISCUSSION

DR. RONALD C. SNIFFEN: At autopsy the patient's abdomen was filled with distended loops of large and small bowel and contained 100 cc of blood-tinged fluid. An 8-cm segment of terminal ileum was gangrenous and was fixed to the sigmoid by fibrinous

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31481

PRESENTATION OF CASE

A forty-year-old man entered the hospital complaining of abdominal distention.

Ten months before admission he had a physical examination and was told that he was in good condition. At that time the liver was palpable two fingerbreadths below the costal margin and a blood smear showed polychromatophilia. During the two months before admission he had lost 14 pounds in weight. One month before admission he complained of drenching night sweats. The liver edge was just below the umbilicus, and the spleen was palpable two fingerbreadths below the costal margin. The lymph nodes were not enlarged. The white-cell count was 20,000, with 30 per cent myelocytes and 2 per cent blast forms, and the red-cell count 3,700,000, with 68 per cent hemoglobin. Three blood examinations later were essentially the same except that the white-cell count rose to 30,000. One week before admission he became nauseated and vomited. He had been constipated, but the abdomen was only slightly distended. The temperature rose to 100°F each evening. A flat plate of the abdomen showed that the liver extended down as far as the pelvis and that the spleen was enlarged. There were several gas-filled loops of small intestine, with no definite obstructive lesion. A barium enema showed no obstruction. The terminal ileum did not fill, and the splenic flexure was depressed by the enlarged spleen. The stools were guaiac negative. Abdominal enlargement progressed, and he was referred to the hospital.

Physical examination revealed an acutely ill and dehydrated man. The tongue was coated and dry. The heart and lungs were normal. The abdomen was distended, with bulging in the flanks. The liver extended into the pelvis, occupying the entire right half of the abdomen. The spleen was two fingerbreadths below the left costal margin.

The temperature was 99°F, the pulse 85, and the respirations 20. The blood pressure was 120 systolic, 85 diastolic.

The urine was negative except for a heavy deposit of amorphous urates. The red-cell count was 3,990,000, with 10.9 gm of hemoglobin. The white-

*On leave of absence.

cell count was 30,400, with 76 per cent neutrophils, 3 per cent myelocytes, 3 per cent myeloblasts, 10 per cent lymphocytes and 8 per cent monocytes. The platelets were normal. The stools were guaiac negative. A flat plate of the abdomen showed numerous loops of dilated small bowel filling the central portion of the abdomen. All the visualized bones were slightly increased in density, with rather coarse trabeculae.

On the second hospital day the patient received 50r of x-ray therapy over the spleen.

The temperature rose to 104°F, and abdominal distention persisted. A Miller-Abbott tube was passed into the jejunum, but x-ray studies showed dilated loops persisting beyond the end of the tube. The temperature dropped rapidly and the pulse became fast and weak. Rales appeared in both lung bases. The patient expired on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. BERNARD JACOBSON: I should like to say at the outset that I am sure that whatever I hazard in the way of diagnosis is going to be wrong. To me, this is an extremely obscure case. There are a few things that I should like to know. In view of the later finding of small-bowel obstruction, I should like to know whether there is any history of a previous abdominal operation. I should also like to know the acid and alkaline phosphatase values, with a view to the question of bone metastases. Finally, it would be of interest to know the morphology of the sternal bone marrow, in view of the question of leukemia.

DR. LEWIS KANE: He had had no abdominal operations. The phosphatase was not done, nor was a sternal biopsy.

DR. JACOBSON: We have a middle-aged man who, ten months before admission, was generally quite well but who had a large liver — or at least a liver that was palpable — and a blood smear that showed polychromatophilia. He went along asymptotically until two months before admission, when he began to have loss of weight, night sweats and fever, an enlargement of the liver and spleen and an increasing degree of small-bowel obstruction. The essential laboratory findings are the x-ray evidence of dilated loops of small bowel, a mild, normochromic or slightly hypochromic anemia and a moderate leukocytosis with a varying proportion of myelocytes, terminally very few, and with apparently no nucleated red cells and normal platelets. This blood picture is certainly a nondescript one.

DR. KANE: There were nucleated red cells.

DR. JACOBSON: That makes the blood picture more suggestive of something I am going to mention soon.

Since time is short I am not going through all the possible diagnoses, but I want to rule out a couple of rather rare conditions. It is possible, I imagine, that this case may have started out fairly asymptotically.

I am going to assume that this was not obstruction from a hernia because I believe that a hernia would have been mentioned if it had been present. I have that amount of confidence in the physical examinations done in this hospital and I assume that the abstractor of the record would not omit such an important fact.

The second commonest cause of small-bowel obstruction is from an adhesive band. We have here

that she had two lesions but we ought to try, if possible, to connect all the events on the basis of one situation.

Another thing in the history that should be noted is the fact that she had black stools. This probably means that she had tarry stools because the stool was positive for blood by a chemical test. Certain conditions occur in the gastrointestinal tract that give blood in the stools whereas some of the others

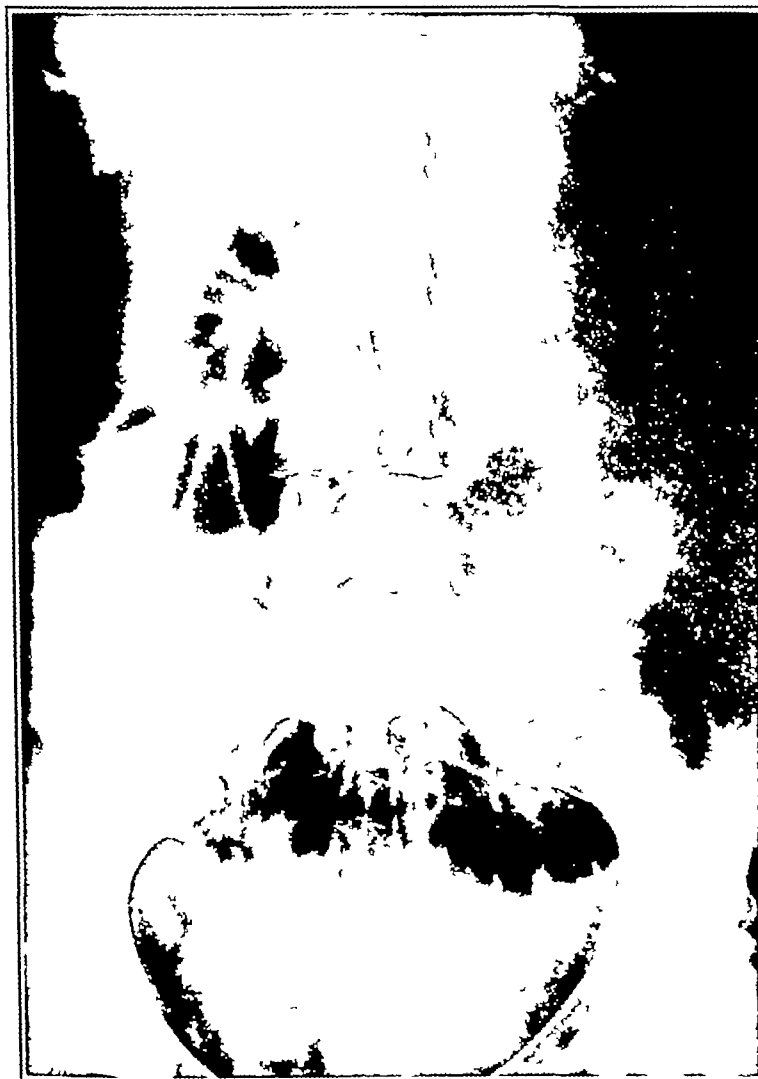


FIGURE 1 *Roentgerogram of the Abdomen*

a history of a hysterectomy done twenty-five years previously. It is not at all infrequent for a knuckle of bowel to become attached to a raw spot of an operative field and to remain symptomless for a period of twenty-five years only to have the adhesive band cross a loop of intestine in such a manner as to produce obstruction comparable to the type that this woman had. The difficulty of making the diagnosis on the basis of an adhesive band is to correlate the seven-month story of symptoms prior to admission. We might assume of course,

are not so apt to do so. One does not often find blood in the stools following small-bowel obstruction associated with strangulated hernia nor with the next commonest cause adhesive band. Two conditions are apt to produce small-bowel obstruction with blood in the stools. The first is intussusception. Quite often in fact practically always I think, bloody stools are one of the chief diagnostic points in making the differential diagnosis of this condition. Intussusception however, does not quite fill the bill on the basis of the previous his-

adhesions. The cause of this gangrene appeared to be thrombosis of the radicles of the superior mesenteric vein, the arteries were patent. The liver weighed 2250 gm but was not otherwise remarkable, the spleen weighed 580 gm, and the pulp was brick red and soft. There were generalized pulmonary edema and congestion, with bronchopneumonia and fibrinous pleurisy in the left lower lobe. The adrenal glands were about three times their normal size, and the medulla of each contained a large blood clot.

Examination of the various tissues microscopically showed changes consistent with leukemia. The bone marrow was hyperplastic, with a predominance of immature cells of the myeloid series, although not to the exclusion of the red-cell elements. The blood vessels in the various organs contained immature white cells, which had also infiltrated the parenchyma of the liver and spleen. The lymph nodes throughout the body were not obviously affected. I cannot connect the two diseases. The infiltration of immature cells in the infarcted terminal ileum was minimal. One does find infarcts in certain organs in leukemia, but it seems to me that for this to have occurred the white-cell count should have been much higher.

CASE 31482

PRESENTATION OF CASE

A fifty-seven-year-old woman entered the hospital complaining of vomiting.

For seven months before admission, she had experienced episodes of epigastric distress and indigestion. During this period she had lost 30 pounds in weight. Three days before admission she awoke with severe, cramping, generalized abdominal pain and vomiting. The pain and vomiting persisted until admission. Her stools were black.

During the year before admission she had noticed moderate dyspnea on exertion and occasional ankle edema. Twenty-five years before admission she had had a hysterectomy.

Physical examination revealed the patient to be well developed and nourished. She vomited brown fecal-smelling fluid almost continuously. The tongue was dry. The heart and lungs were negative. The abdomen was distended and diffusely tender. An old suprapubic scar was present. Pelvic examination was negative.

The temperature was 98°F, the pulse 100, and the respirations 22. The blood pressure was 120 systolic, 75 diastolic.

The urine gave a + test for acetone, and the sediment contained 1 or 2 white cells and a rare red cell per high-power field. The red-cell count was 5,130,000, and the white-cell count 22,500. The stool was guaiac positive, and the vomitus guaiac negative.

A flat plate of the abdomen showed dilated loops of small bowel (Fig 1). A barium enema revealed no evidence of obstruction of the large bowel.

Soon after admission, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR ARTHUR W ALLEN We might look at the x-ray films.

DR CLAYTON H HALE This film shows the dilated loops of small bowel described in the original report. The films of the barium enema rule out any obstruction in the colon, the defects demonstrated are due to gas and fecal material. The terminal ileum did not fill.

DR ALLEN Do you see any evidence of foreign body?

DR HALE No foreign body is apparent.

DR ALLEN We have a patient with obvious small-bowel obstruction. Not only is this obvious but it is apparent that the obstruction was low in the small intestine. It was low because, although she had been acutely ill for three days, she was still not a very sick patient when she was admitted. Had this obstruction been higher she would either have been dead or would have been admitted to the hospital sooner. Another reason why the obstruction must have been low is that the vomitus described was fecal in character. One must, however, take into consideration the possibility of actual fecal material in the stomach by the way of a perforation through a tumor of the colon into the stomach. Tumors almost never perforate from the stomach into the bowel, but they quite often do so from the bowel into the stomach. This idea might be toyed with as a possibility, but if such a condition had been present, one would have difficulty in explaining the obvious small-bowel obstruction. Under such circumstances she would have decompressed the intestine through the fistula into the stomach and an associated small-bowel obstruction of this extent would probably not have been present.

We must consider that part of the history which states that for seven months before admission she had had attacks of epigastric distress and indigestion. Also, this had disturbed her sufficiently, I assume, to account for the 30-pound loss in weight. All the common causes of small-bowel obstruction that I know about are quite apt to be associated with a prolonged history of epigastric distress with weight loss.

The most frequent cause of small-bowel obstruction is strangulated hernia. The fact that hernia is not mentioned in this case does not rule it out, because approximately 30 per cent of patients who come to the hospital with small-bowel obstruction from a strangulated hernia do not refer their pain to the region of the hernia, even if they know that they have one, and quite often a hernia may be overlooked in the routine examination of that region.

I am going to assume that this was not obstruction from a hernia because I believe that a hernia would have been mentioned if it had been present. I have that amount of confidence in the physical examinations done in this hospital and I assume that the abstractor of the record would not omit such an important fact.

The second commonest cause of small-bowel obstruction is from an adhesive band. We have here

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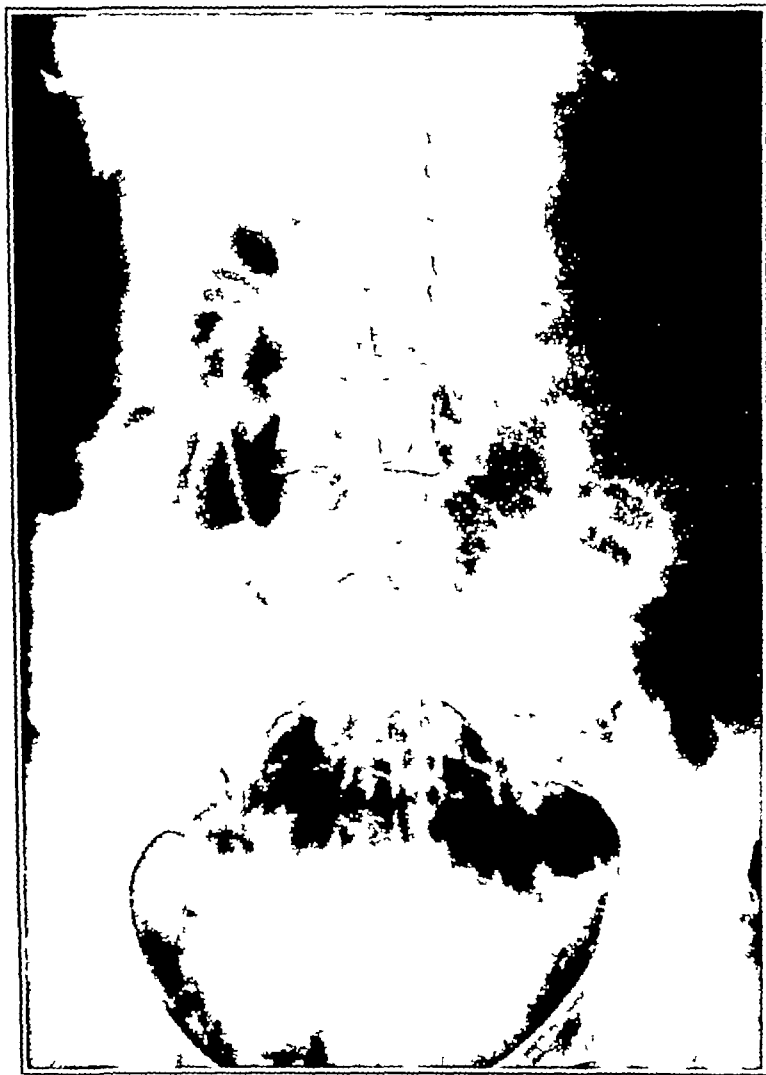


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of a man who, for some reason had swallowed two halves of an orange separately when these got together in the terminal ileum intestinal obstruction occurred. I can recall another case of intestinal obstruction in a man who had accidentally swallowed a whole wooden toothpick, this had extruded itself through one loop of terminal ileum and had pinned itself into another loop in such fashion that it produced intestinal obstruction. There are other rare conditions that may account for a picture of this sort but I shall go back to the most frequent cause that fulfills all the requisites, I believe that this woman had a Meckel's diverticulum containing gastric mucosa.

CLINICAL DIAGNOSIS

Intestinal obstruction

DR ALLEN'S DIAGNOSIS

Acute small-bowel obstruction (terminal ileum) based on a Meckel's diverticulum containing gastric mucosa

ANATOMICAL DIAGNOSIS

Leiomyoma of terminal ileum

PATHOLOGICAL DISCUSSION

DR RONALD C SNIFFEN The surgeon resected 14 cm of terminal ileum. Budding from the wall of its midportion was a 13-by-5 cm, grossly lobulated, encapsulated, firm tumor, with a pale-gray to yellow glistening cut surface marked by hemorrhagic and gelatinous areas (Fig 2). There was a diverticulum of the intestinal wall that extended for 1 cm into the substance of the tumor, the diverticulum measured 7 mm in diameter. There was mucosal hemorrhage in the depths of the diverticulum, at which point the mucosa seemed to be ulcerated. The microscopic diagnosis of the tumor was leiomyoma.

According to Ewing,³ this type of diverticulum is not infrequent with leiomyomas of the intestine, therefore I do not believe that it represents a pre-existing diverticulum.

DR ALLEN Did the tumor arise in the bowel or outside?

DR SNIFFEN In the bowel wall. It had no attachment to any other organ.

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2. Stallo F A, Fier S A, and Carr I B. Primary malignant disease of small intestine. *Am J Sur* 69:572-583, 1945.
3. Ewing J. *Neoplastic Diseases: A treatise on tumors*. 1160 pp. Philadelphia: W B Saunders Company, 1942. P 27.

tory It is a little difficult to picture a woman with seven months of indigestion and epigastric distress due to recurrent or partial intussusception, which finally became complete. The other lesion that produces the symptoms and signs of small-bowel obstruction associated with blood in the stools is a Meckel's diverticulum. In people of this age it is a little less frequent than in children. A large percentage of the patients with Meckel's diverticulum have gastric mucosa in the diverticulum, and they often develop a peptic ulcer in this gastric mucosa, which may cause blood in the stools. Furthermore, they may well have a history of indigestion for a

ileus cannot be completely ruled out. There has been a recent report of a seventy-five-year-old man with a history not unlike this — weight loss and indigestion for a long period of time — who had a true calculus in the terminal ileum.¹ This was not a gallstone but was composed of calcium carbonate and calcium phosphate and showed up clearly in the x-ray film.

One should also consider the possibility of small bowel malignant tumor, although such tumors are rare. Dr. Shallow and his colleagues,² of Philadelphia, were able to collect from the literature about 300 cases of malignant disease of the small



FIGURE 2 Photograph of the Tumor of the Ileum
The arrow points to the diverticulum.

period of seven or eight months, which would be sufficient to account for weight loss that occurred in this case. The majority of patients with Meckel's diverticulum who enter this hospital in the acute phase are diagnosed preoperatively as cases of intestinal obstruction. Very rarely is the diagnosis made in the adult prior to exploration.

I shall mention two or three less frequent conditions that might be thought of under these circumstances. The seven-month period of indigestion prior to admission would go perfectly well with gallstones, even to the point of weight loss. There is, however, no evidence of gallstones in the region of the gall bladder, and Dr. Hale assures me that there is no shadow in the affected area that might be interpreted as a gallstone. Since gallstones are frequently not visible in the x-ray film, gallstone

intestine. These lesions actually accounted for only 0.01 per cent of the cases of malignant tumor of the gastrointestinal tract.

One sees a good many cases of a benign tumor of the small bowel that produces intussusception, and that must be considered here as a possibility. If it were a polypoid lesion it would also account for the bleeding, whether or not intussusception was present. I recently had a case with a condition that only rarely produces intestinal obstruction. In this patient there was a large tumor attached to the terminal ileum that had become necrotic owing to a twisted pedicle or possibly to a thrombosis of the blood supply. This situation produced symptoms not unlike those described here. We have had cases with foreign bodies of all varieties that produced intestinal obstruction. One case I remember vividly was that

in its place only dreadful uncertainty, we must turn to our peacetime environs and pursuits and evaluate their possibilities for danger. In this competition,—if the idea of competition can be further tolerated,—the Metropolitan Life Insurance Company* presents as a candidate the American home, which claims around 32,000 lives a year, of which some 24,000 are those of adults. The home cannot rank with the battlefield as an amphitheater for the exhibition of courage, but if the truth is known,—and the Metropolitan Life Insurance Company seems determined on making it known,—brave men may well hesitate before setting foot upon the familiar doorstep.

Falls lead the list in the production of injuries in the group from fifteen to sixty-nine years, as has probably been the case since Newton discovered the law of gravity, and before here, too, man's ingenuity has been responsible for his downfall, and ladders and stairs have made their contribution to the list of broken heads and other fractured appendages. It is so with all our inventions. Since the development of the wheel, marking the first great turning point in man's progress, man has been broken on or by the wheel.

Burns, as a result of conflagration and otherwise, come second in the list of types of accidents causing fatal injuries in the home. After them, in order of frequency, come absorption of poisonous gas, acute poisoning, injury by firearms and other causes. Apparently the American home, as inhabited by Americans, is a hazardous place in which to spend one's spare time.

That the bedroom was found to be the part of the house where the greatest number of fatalities occur is not surprising, since the majority of people

still die in bed. The difficulty encountered in getting children off to bed shows, perhaps, that they are instinctively aware of the risk involved.

Aside from fatal accidents, and including all age groups, a list of the more frequent accidents sustained in the home and the type of carelessness contributing to them should occasionally be made available. Here would be included cuts from broken glass and from the opening of cans with improper

instruments, the exploration, by children, of too easily available medicine closets, the use of infant sleeping bags that close too tightly about the neck and, to return to falls, the slipping of bathinettes precariously set up in bathtubs, the spreading of unanchored rugs on waxed floors and the parking of divers parcels on stairs.

Accidents are bound to occur in and about

the home because so many of our activities are centered there. Reasonable precautions, however, could offset many of these risks and make the home more truly the secure sanctuary that we like to consider it.

MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to

George L. Schadt, *Chairman*
Postwar Loan Fund
8 Fenway
Boston 15, Massachusetts

MEDICOLEGAL ABSTRACT

Relation of Patient and Physician Liability for malpractice. Malpractice cases, as do all cases of negligence, require proof that the defendant was negligent and that his negligence caused the plaintiff's injury, that is, the case for the plaintiff on either issue is usually established by expert testimony. Whether or not a doctor or a dentist used skill and methods meeting the required standards of care and whether or not there was causal connection between the care or lack of care for which a doctor or dentist was responsible are also matters that usually can be established only by expert testimony. There have been some exceptions to this rule in cases in which the court has believed that the evidence was such that a layman could properly form an opinion without the aid of expert testimony.

In one such case recently decided by the Supreme Court of Massachusetts, the plaintiff presented no

*Hazardous areas in and about home. *Statistical Bulletin Metropolitan Life Insurance Company* 26:8 (Sept.), 1945

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THE CHRISTMAS SEAL CAMPAIGN

THE development of mass radiography is sure to be counted as one of the outstanding landmarks in the control of tuberculosis. Its revelation of additional thousands of cases of the disease may have been momentarily disquieting, but a tremendous field of improvement has been opened for reducing the percentage of far-advanced cases, and achieving a corresponding increase of those caught while still in the minimal stage.

Mobile x-ray units operated by the United States Public Health Service in various parts of the country found that 3 in every 200 persons examined gave evidence of reinfection tuberculosis — active or inactive. Sixty-five per cent of the lesions were in

the minimal stage, 30 per cent in the moderately advanced stage, and 5 per cent in the far-advanced stage. Preinduction examinations by the Selective Service alone revealed 150,000 cases with x-ray evidence of the disease.

In industrial surveys an overwhelming number of workers who could afford private care designated their family physicians as those to whom the report of the x-ray findings should be made — these reports being accompanied by a request for further clinical studies. Provided that these physicians possess a sufficiently broad understanding of tuberculosis and modern therapeutic methods, this means that sanatorium care will become secondary to outpatient supervision and to treatment by the physician. As mass radiography units penetrate all sections of the country, the demand for this type of care will of course be greatly increased.

Through its vast nationwide educational program and case-finding and rehabilitation work, the National Tuberculosis Association and its affiliated groups will continue to awaken communities to the dangers of the disease. As a result, these communities will find it necessary to provide the armamentarium needed for the proper care of the tuberculous patient. Since such activities are supported by the sale of Christmas Seals, it behooves all those interested in the conquest of the tuberculosis menace to buy as largely of the seals this season as their resources will permit. Such support means an expansion of clinical, field-service and laboratory facilities, well equipped sanatoriums accessible to population centers and additional aids for the physician not only to control but also to eradicate the "white plague" within a reasonable time.

"HOW SLEEP THE BRAVE —

"Courage," according to Noah Webster, is that firmness of spirit which meets danger without fear. Bravery is daring, often defiant courage. The late Ernie Pyle in his book *Brave Men* gives many examples of both types — courage as a spiritual quality, and bravery as so often shown under the stress of combat.

With the loss of opportunity for exhibiting courage sustained by the ending of the war, which has left

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THE ROLE OF SYMPATHECTOMY IN THE TREATMENT OF IMMERSION FOOT AND FROSTBITE*

JAMES L. SOUTHWORTH, M.D.†

BALTIMORE, MARYLAND

THE term "frostbite" designates the lesions produced by exposure to cold. Short exposure to extremely low temperatures or longer exposure to moderately low temperatures results in similar conditions, although damage appears to be more localized when caused by low-temperature exposures of short duration.¹ During World War II many cases have resulted from prolonged soaking of the feet in cold water, hence the term "immersion foot." In this connection White² draws a distinction between the lesions of immersion foot and those caused by prolonged exposure in southern latitudes coupled with nutritional deficiencies. Many patients with frostbite or immersion foot have late sequelae and present problems of treatment, disability evaluation and rehabilitation. With regard to treatment, the question concerning the value of sympathectomy arises.³

PATHOLOGY

Histologic changes in human tissue due to cold have been described.⁴⁻⁶ In the acute phase there is damage to the endothelium of the smaller vessels and extravasation of fluid. Some workers have demonstrated degenerative changes in small nerve fibers.⁷ Tissue necrosis occurs if exposure has been severe. If infection supervenes, its characteristic changes are added to the picture. The skin in any event usually shows more or less superficial areas of necrosis, but if infection can be avoided the lesions have a tendency to heal better than would be expected from the clinical findings. The healing process is characterized by an abundance of fibrosis involving all the tissues of the hand or foot,^{8, 9} a change that apparently accounts for the late symptoms.

THE ACUTE PHASE

The clinical picture of the acute phase is fairly characteristic. During exposure the extremities

become numb and painless. No covering except hip boots or a full rubber suit prevents immersion foot, and even with this protection frostbite may be sustained in Arctic waters. Constricting bands that slow circulation are said to increase the severity of the lesions. Application of grease to the feet gives only slight protection during exposure.

When the feet begin to warm after rescue, they lose their pallor, and redness, edema and ecchymosis appear. Pain is prominent during the early recovery period and in higher environmental temperatures is severe. It is inadvisable to warm the feet suddenly after exposure, and the best first aid is exposure of the feet in a cool compartment.

Within a day or two the changes become fully developed and the extent of injury may be estimated.

Brownrigg⁹ divides cases of immersion foot or frostbite into first-, second- and third-degree types. The first-degree type represents a minimal lesion. There is edema of the foot and sometimes of the ankle and leg, with ecchymosis, hyperemia and bleb formation. There is considerable pain, but the skin may show diminished sensation as high as the knees. The course is relatively benign unless infection develops. Swelling, hyperemia and pain gradually subside, and cutaneous sensitivity in the leg and ankle regresses. Superficial plaques of dry, gangrenous skin may remain on the tips of the toes or on the foot. These fall away, leaving pink new skin. With proper treatment many first-degree cases heal without any residual disability in about six weeks. Approximately 25 per cent of such patients have bothersome complaints of a neuritic or vasospastic nature.

In second-degree cases, all the lesions noted in the first-degree type are present, together with death of tissue in the distal parts of the extremity, involving both the skin and the subcutaneous tissues. Circumscribed gangrene of the toes is frequent. Occasionally the entire distal portion of the foot is affected. This degree of injury heals as does the first-degree type in so far as the acute manifestations are concerned. Isolated areas of gangrene, either dry or infected, remain, necessitating amputa-

*From the surgical services of the United States marine hospitals at Staten Island, New York, and Savannah, Georgia. Published with permission of the Surgeon General of the United States Public Health Service.

†Sergeon, Division Marine Hospitals, United States Public Health Service.

expert opinion on the issue either of negligence or of causal connection

In April, 1940, the defendant, a dentist, extracted sixteen of the plaintiff's teeth. As a result of the extraction the plaintiff was nauseated and bled profusely. She returned home and remained there for several days, suffering from constant pain in the chest and a bad cough. During the next fifteen months the chest was sore and she had coughing spells and occasional hemorrhages. X-ray films were taken at various times during that period. About fifteen months after the extraction of her teeth, the plaintiff, during a coughing spell, coughed up a tooth, whereupon her disfigurement disappeared and her health became normal. Re-examination of the x-ray films showed that a tooth fragment had been lodged in the left lower bronchus. The plaintiff had received no dental treatment between the time that the defendant had worked on her and the time that she had coughed up the tooth fragment. The plaintiff presented no evidence by any expert that the defendant's treatment was not in accordance with proper dental standards.

The defendant rested his case without introducing any evidence, and the court directed a verdict in his favor. On appeal, the Supreme Judicial Court held that the action of the lower court was erroneous, saying in part

This is not a case where a finding of negligence must rest on mere conjecture. [Citations omitted.] We have not overlooked the fact that the plaintiff offered no expert evidence on the issue of the defendant's negligence. Ordinarily a jury is not permitted without the aid of expert evidence to determine whether the conduct of a dentist or physician is a breach of the duty owed to a patient. [Citations omitted.] But, although exceptional, the facts in a malpractice case may be such that jurymen out of their common knowledge and experience are able to pass on this question. — (*Malone v. Bianchi* [May 3, 1945], Mass. Adv. Sh. [1945], 559.)

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Salem	December 3	Paul W. Hugenberger
Haverhill	December 5	William T. Green
Lowell	December 7	Albert H. Brewster
Brockton	December 13	George W. Van Gorder
Pittsfield	December 17	Frank A. Slowick
Fall River	December 17*	Eugene A. McCarthy
Springfield	December 18	Garry deN. Hough
Hyannis	December 18*	Paul L. Norton
Worcester	December 21	John W. O'Meara

Physicians referring new patients to clinic should get in touch with the District Health Officer to make appointments.

*Day changed

NOTICES

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9-10 a.m.

MEDICAL CONFERENCE PROGRAM

- Wednesday, December 5 — Tonsils and Aging Dr. George Kelemen
Friday, December 7 — The Nature of Some Diseases Ascribed to Disorders of the Lipid Metabolism Dr. Sidney Farber
Wednesday, December 12 — Anti-Hormones Dr. Kenneth W. Thompson
Friday, December 14 — Some Clinical Considerations of Louse-Borne Typhus Lt. Comdr. Andrew Yeomans, U.S.A. Typhus Commission
Wednesday, December 19 — Slipping Epiphysis of the Head of the Femur in Growing Children Dr. Russell Sullivan
Friday, December 21 — The Clinical Evaluation of an Anti-Hemophilic Fraction of Plasma Dr. Louis K. Diamond

On Tuesday and Thursday mornings Dr. S. J. Thannhauser will give medical clinics on hospital cases. On Saturday mornings, clinics will be given by Dr. William Dameshek.

All morning conferences are open to the medical profession.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, December 6, at 7:15 p.m. in the classroom of the Nurses' Residence. Dr. Harold J. Jeghers will speak on the subject "Practical Points on Malaria and Amebiasis." Dr. Isabel S. Money will be chairman.

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, December 11, at 8:15 p.m. Dr. Frank H. Lahey will speak on the subject "Lesions of the Terminal Ileum, Colon and Rectum."

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, DECEMBER 6

THURSDAY, DECEMBER 6

7:15 p.m. Monthly clinical conference and meeting of the staff, New England Hospital for Women and Children

FRIDAY, DECEMBER 7

*9:00-10:00 a.m. The Nature of Some Diseases Ascribed to Disorders of the Lipid Metabolism Dr. Sidney Farber, Joseph H. Pratt Diagnostic Hospital

*9:00-10:00 a.m. Medical clinic, Isolation Amphitheater, Children's Hospital

*10:00 a.m.-12:00 p.m. Medical staff rounds, Peter Bent Brigham Hospital

10:50 a.m. Vesicular and Bullous Eruptions of the Skin Dr. Bernard Appel (Postgraduate clinic in dermatology and syphilology) Amphitheater, Dowling Building, Boston City Hospital

MONDAY, DECEMBER 10

*12:00 p.m.-1:00 p.m. Clinicopathological conference, Peter Bent Brigham Hospital

TUESDAY, DECEMBER 11

*9:00-10:00 a.m. Medical clinic, Infants Hospital

*12:15-1:15 p.m. Clinicorontgenological conference, Peter Bent Brigham Hospital

8:00 p.m. Harvard Medical Society Amphitheater, Peter Bent Brigham Hospital

8:15 p.m. Greater Boston Medical Society Auditorium, Beth Israel Hospital

WEDNESDAY, DECEMBER 12

*9:00-10:00 a.m. Anti-Hormones Dr. Kenneth W. Thompson, Joseph H. Pratt Diagnostic Hospital

(Notices continued on page xvii)

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THE ROLE OF SYMPATHECTOMY IN THE TREATMENT OF IMMERSION FOOT AND FROSTBITE*

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BALTIMORE, MARYLAND

THE term "frostbite" designates the lesions produced by exposure to cold. Short exposure to extremely low temperatures or longer exposure to moderately low temperatures results in similar conditions, although damage appears to be more localized when caused by low-temperature exposures of short duration.¹ During World War II many cases have resulted from prolonged soaking of the feet in cold water, hence the term "immersion foot." In this connection White² draws a distinction between the lesions of immersion foot and those caused by prolonged exposure in southern latitudes coupled with nutritional deficiencies. Many patients with frostbite or immersion foot have late sequelae and present problems of treatment, disability evaluation and rehabilitation. With regard to treatment, the question concerning the value of sympathectomy arises.³

PATHOLOGY

Histologic changes in human tissue due to cold have been described.⁴⁻⁶ In the acute phase there is damage to the endothelium of the smaller vessels and extravasation of fluid. Some workers have demonstrated degenerative changes in small nerve fibers.⁷ Tissue necrosis occurs if exposure has been severe. If infection supervenes, its characteristic changes are added to the picture. The skin in any event usually shows more or less superficial areas of necrosis, but if infection can be avoided the lesions have a tendency to heal better than would be expected from the clinical findings. The healing process is characterized by an abundance of fibrosis involving all the tissues of the hand or foot,^{8, 9} a change that apparently accounts for the late symptoms.

THE ACUTE PHASE

The clinical picture of the acute phase is fairly characteristic. During exposure the extremities

become numb and painless. No covering except hip boots or a full rubber suit prevents immersion foot, and even with this protection frostbite may be sustained in Arctic waters. Constricting bands that slow circulation are said to increase the severity of the lesions. Application of grease to the feet gives only slight protection during exposure.

When the feet begin to warm after rescue, they lose their pallor, and redness, edema and ecchymosis appear. Pain is prominent during the early recovery period and in higher environmental temperatures is severe. It is inadvisable to warm the feet suddenly after exposure, and the best first aid is exposure of the feet in a cool compartment.

Within a day or two the changes become fully developed and the extent of injury may be estimated.

Brownrigg⁹ divides cases of immersion foot or frostbite into first-, second- and third-degree types. The first-degree type represents a minimal lesion. There is edema of the foot and sometimes of the ankle and leg, with ecchymosis, hyperemia and bleb formation. There is considerable pain, but the skin may show diminished sensation as high as the knees. The course is relatively benign unless infection develops. Swelling, hyperemia and pain gradually subside, and cutaneous sensitivity in the leg and ankle regresses. Superficial plaques of dry, gangrenous skin may remain on the tips of the toes or on the foot. These fall away, leaving pink new skin. With proper treatment many first-degree cases heal without any residual disability in about six weeks. Approximately 25 per cent of such patients have bothersome complaints of a neuritic or vasospastic nature.

In second-degree cases, all the lesions noted in the first-degree type are present, together with death of tissue in the distal parts of the extremity, involving both the skin and the subcutaneous tissues. Circumscribed gangrene of the toes is frequent. Occasionally the entire distal portion of the foot is affected. This degree of injury heals as does the first-degree type in so far as the acute manifestations are concerned. Isolated areas of gangrene, either dry or infected, remain, necessitating amputa-

*From the surgical services of the United States marine hospitals at Staten Island, New York, and Savannah, Georgia. Published with permission of the Surgeon General of the United States Public Health Service.
†Surgeon, Division Marine Hospitals, United States Public Health Service.

tion of one or more toes. If chronic ulceration of a toe develops, the distal portion of the digit must be amputated, although conservative treatment is in order. The acute phase may be said to be complete when all ulcers or gangrenous areas have been cured, by amputation or otherwise, which requires about three months. Approximately 75 per cent of these patients have annoying complaints of a neuritic or vasospastic nature in addition to any disability that may be caused by the loss of toes.

Third-degree immersion foot or frostbite includes the cases that develop gangrene in the deeper tissues proximal to the toes and those in which there is widespread damage to the skin and deeper structures. It includes all the severest cases, such as those with complete gangrene of the foot. Secondary infection is the rule, so that toxic systemic reaction is almost invariably present. Amputation above the ankle is usually required. It must be noted, however, that conservatism is indicated both concerning the time and the selection of the level of amputation. This has been emphasized in a recent report by Lesser.⁸ Because amputations are obligatory, late neurologic and vasospastic complications are absent, disability results from amputation alone.

Treatment

The purposes of early treatment are to prevent further damage to tissues in a precarious metabolic state, to relieve pain and to protect the patient as far as possible from toxemia.

Cooling of the parts relieves pain and possibly aids tissue survival through lowering metabolic requirements so that impaired circulation is more nearly adequate. The patient is placed at bed rest as soon as possible after rescue, and the affected parts are protected from trauma by a cradle. Active cooling may then be employed. Two convenient methods are recommended.² If the local manifestations are not severe, the member may be swathed in thick bandages and covered with several ice bags. If open lesions or great swelling and discoloration are present, the patient is more comfortable when cooling is carried out by means of a fan at the lower end of a cradle. Sterile water or saline solution may be sprayed over the feet from time to time. The temperature of the skin should be between 75 and 85°F.

If there is evidence of pre-existing dermatophytosis, daily soaks in cool potassium permanganate solution should be employed, other factors permitting. Routine administration of sulfonamide or penicillin seems justified to prevent or combat infection. Inspection for evidence of thrombophlebitis should be made twice daily and appropriate measures instituted early.

If the lesion is third degree, infection and tissue damage progress in spite of treatment. When it becomes obvious that the tissues will not heal or

when the general condition demands it, amputation should be performed. Refrigeration anesthesia with amputation near the affected level is advisable, the simplest operation is employed and is followed by skin traction. If the patient is received in poor general condition owing to infection and gangrene of a foot, a tourniquet should be applied near the infected site and the lost tissue should be refrigerated until the general condition is improved.

The lesions of frostbite produced without the wetting factor may be the same as those of immersion foot, particularly when there has been prolonged exposure to cold without opportunity to change the socks. Trench foot, a closely related lesion, sometimes resembles dry frostbite and sometimes immersion foot, depending on the amount of wetting.^{8, 10} Ordinary civilian-type frostbite tends to be less diffuse. As was mentioned previously, high-altitude frostbite also seems to produce more localized severe lesions. In my experience, the late sequelae described below have been less prominent in civilian-type lesions. When present they tend to be localized to one or two digits and may be cured by amputation of the distal part of the digit. Otherwise, the clinical course and treatment of trench foot and localized frostbite are similar to those of immersion foot.

LATE MANIFESTATIONS

The late manifestations of immersion foot or frostbite fall into three principal groups: disturbances of cutaneous sensation, inadequate circulation and pain on use.

Disturbances of Cutaneous Sensation

Disturbances of cutaneous sensation are of two kinds, both often being present in the same patient. In all but the mildest cases there is some residual anesthesia or hypesthesia of the skin. As was noted, this may extend to the knee or above in the early stage, but it spontaneously recedes, leaving distal areas of the foot affected. In the chronic state it is usually confined to the plantar surface in the region of the ball of the foot. It may range from complete insensibility to all modalities to dissociation of touch from pain and temperature sense. This symptom tends to run a prolonged course, but makes further spontaneous improvement from the third to the twelfth month. In some patients the dorsal surfaces of the toes remain insensitive for years. Anesthesia of the skin does not, however, seem to constitute a source of annoyance or disability to the average patient.

The second type of disturbance of sensation is hyperesthesia. It may be found in zones adjacent, and usually proximal, to anesthetic areas, and in some first-degree cases is the only evidence of nerve dysfunction. It consists of hyperirritability to ordinary stimuli. The plantar reflex is exaggerated,

and the patient is annoyed by the weight of bed-clothes or by walking. The reactions to the varying disability that this symptom creates are mixed. To some patients it is disagreeable, especially when walking, others scarcely notice it except when trying to sleep, still others know that it is present but are not disturbed by it. Although these sensations may be painful, they should be clearly differentiated from the pain described below.

In old, untreated cases of immersion foot, trophic ulcers — so-called "perforating ulcers" — may appear. They are usually precipitated by some local trauma, such as a fracture, but tend to persist after the acute injury has healed. The site is in hyperkeratotic skin of the sole. These lesions are resistant to treatment. They may be in some way associated with persistent disturbance of cutaneous sensation.

Inadequate Circulation

Inadequate circulation as a sequel of immersion foot or frostbite varies from patient to patient, being absent, transient or barely perceptible in some cases and quite prominent in others. The factors influencing its incidence and severity are obscure. It is not necessarily connected with length of exposure, and may be associated with inherent sensitivity of the vasomotor apparatus. Hyperhidrosis is a frequent symptom. At varying periods during the day, particularly in the early morning, the feet are cold, wet and pallid, and beads of perspiration stand out across the volar surface. Attacks of pallid or blue cyanosis with mottling of the skin may occur on exposure to cold. Following such a period, there is sometimes mild hyperemia. These symptoms are not associated with pain at rest, but are unpleasant and annoying. Quantitative studies of extremity circulation in old cases of untreated immersion foot show diminished flow when compared with sympathectomized extremities in the same patients,¹¹ both extremities originally showing almost identical effects of exposure.¹²

A less frequent symptom of circulatory disturbance is intermittent claudication. It is similar to the corresponding symptom seen in arteriosclerosis, with the exception that it tends to regress spontaneously. Other changes often noted in connection with vasospastic diseases sometimes occur in immersion foot twelve to eighteen months after injury. In an appreciable number of patients the skin of one or more digits becomes atrophic, thin, red and glistening. It is less pliable than normal, fissures and cracks may occur and lead to late ulcerations, not necessarily on the tips of the digits but often in creases about the joints. If the fingers have been affected, contractures and a thin atrophic digit may result, requiring amputation long after the acute stage of the disease has passed.

Intolerance to cold is associated with circulatory changes following frostbite or immersion foot. In

untreated cases, cold brings on numbness and tingling. This, together with decrease in agility of the part, especially in the hand, constitutes a disability.

Pain on Use

Pain in the feet on walking in immersion foot and to a lesser extent pain on use of the hands in frostbite — not necessarily associated with cold — is the principal disabling factor. Long after cutaneous sensation has returned to normal and circulatory disturbances have been relieved, pain may persist. This type of pain is to be differentiated from the various painful sensations described above that may arise in connection with other sequelae. It is dull and aching and is deep-seated, seeming to the patient to be situated in the bones and joints. It is brought on by weight-bearing or work and is relieved by rest. There is associated stiffness of the various joints and loss of normal pliability of the structures. A peculiar waddling gait results. This symptom is probably related to the increased fibrosis that follows exposure to cold.⁵ In the hand it is represented by a tendency to tire quickly, but is much less frequently seen there.

It should be noted that the victims of immersion foot in particular have associated neuropsychiatric disturbances, which are not, however, related to exposure to cold *per se*. These vary from acute mild episodes of nervousness and irritability to chronic and severer personality disorders. Neuropsychiatric symptoms may overshadow the local organic lesions and render rehabilitation difficult. When these symptoms are present, treatment should of course be primarily directed toward this condition, but local measures need not be neglected.

SYMPATHECTOMY

The role of sympathectomy in the treatment of acute immersion foot or frostbite is debatable. In civilian frostbite involving only one or two digits, sympathetic block with Metycaine Hydrochloride seems to hasten healing and to have no ill effect. In more diffuse lesions resulting from exposure to dry cold, repeated sympathetic blocks apparently hasten healing. This is illustrated by the following cases.

Three merchant seamen were cast adrift for three days on the after half of a ship without heating and with few shelter facilities. The air temperature probably varied from 10 to 30°F. The factor of wetting was not prominent during this exposure. When the men were admitted to the hospital, the lesions comprised first-degree frostbite, with edema, ecchymosis and moderate discoloration of the hands. There were blisters at the tips of several digits in each patient. The patients were treated with repeated sympathetic blocks every third or fourth day for three to five treatments each. Dry plaques

tion of one or more toes. If chronic ulceration of a toe develops, the distal portion of the digit must be amputated, although conservative treatment is in order. The acute phase may be said to be complete when all ulcers or gangrenous areas have been cured, by amputation or otherwise, which requires about three months. Approximately 75 per cent of these patients have annoying complaints of a neuritic or vasospastic nature in addition to any disability that may be caused by the loss of toes.

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equelae of frostbite or immersion foot, however, sympathetic-nerve block or ganglionectomy appears to be indicated. The clinical features of the cases on which this assumption is based are summarized in the accompanying tables.

It is a singular fact that the disturbances of cutaneous sensitivity are almost invariably removed by sympathectomy. In some patients a temporary sympathetic block not involving the somatic nerves immediately restores cutaneous sensitivity and relieves hyperesthesia. In others there is a return to normal within two or three days after ganglion block by alcohol injection or ganglionectomy, but it should be noted, as already stated, that these symptoms do not usually contribute much to permanent disability. One would hesi-

performed. Otherwise alcohol block may be used for symptomatic relief.

Deep-seated pain, which is often the principal disabling symptom, does not respond to sympathectomy. It appears to be made neither worse nor better. Nor has it, in my experience, been helped by physiotherapy or mechanical appliances for the feet. With time the pain becomes much dulled or the patient becomes accustomed to it, but in some cases it is still so severe after three years that it constitutes a partial disability requiring change of occupation.

Lumbar Sympathectomy and Sympathetic Block

The sympathetic fibers that control the blood vessels of the lower extremities arise in the thoracic

TABLE 2 Summary of Data on Patients with Frostbite

CASE No	NATURE OF EXPOSURE	DEGREE	DURATION OF SYMPTOMS ON ADMISSION	SYMPTOMS	TREATMENT	RESULT
1	In air temperature of 10°F for 8 hr (1935)	3rd (8 fingers)	7 yr	Stiffness and pain in hands on exposure to cold	Repeated procaine blocks (previous treatment had included amputation and grafts)	No improvement
2	Worked all day standing on ice (1933)	2nd (both feet)	9 yr	Vasospasm and ulceration of toes, trophic ulcer of sole	Sympathectomy	Toes healed, trophic ulcer remained
3	3 days in air temperature of 20-30°F (1943)	1st (4 fingers)	Immediate	Dry gangrene of fingertips, hyperhidrosis + + + +	Repeated procaine blocks	Apparently cured, returned to duty after 6 wk. re-exposure caused contracture of little finger
4	3 days in air temperature of 20-30°F (1943)	1st (2 fingers)	Immediate	Dry gangrene of fingertips, hyperhidrosis + + + +, hyperesthesia +	Repeated procaine blocks	Apparently cured in 8 wk
5	3 days in air temperature of 20-30°F (1943)	1st (6 fingers)	Immediate	Dry gangrene of fingertips, hyperhidrosis + +, anesthesia in fingers + +	Repeated procaine blocks	Apparently cured
6	Shovelled for 3 hr at temperature of 20°F	2d (2 fingers)	Immediate	Acute swelling of hand, ulceration of 2 fingers	Physiotherapy	Amputation of tips of fingers, moderate stiffness of fingers
7	Worked for 4 hr on metal parts in air temperature of 30°F (12/42)	2nd (1 finger)	10 mo	Intolerance to cold + + + +, chronic fissures and ulceration, stiffness of distal joint	Alcohol sympathetic blocks	Ulcer healed but pain remained, end of finger amputated with cure

tate to recommend bilateral ganglionectomy for relief of these symptoms alone. If a block lasting six to eight months can be performed by alcohol injection, it is worth while. Recurrence of sympathetic activity is not associated with return of these symptoms. If the symptoms are particularly distressing and if it is impossible to obtain satisfactory alcohol block, as it is in some cases, sympathectomy is justified.

If persistent and annoying symptoms of circulatory insufficiency resembling vasospasm are present, sympathectomy is helpful. If excessive sweating, Raynaud's phenomenon or intermittent claudication is prominent in the clinical picture, sympathectomy results in marked improvement. Since these symptoms tend to regress spontaneously, the decision to perform sympathectomy may be safely postponed. If thinning of the skin appears within the first three months, sympathectomy should be

and the lumbar and perhaps the sacral segments. Extirpation of the first, second and third lumbar ganglions produces satisfactory sympathetic denervation in the lower extremity. There are interlacing fibers on the anterior surfaces of the bodies of the lumbar vertebrae, and a few patients seem to have some crossing of innervation, at least paravertebral blocks of the second and third ganglions of one side — using 2 cc of 2 per cent procaine to each ganglion, amounts presumably not large enough to diffuse to the opposite side — sometimes produce vasodilator effects on the opposite side. In one patient, however, in whom this effect was constant on several occasions and who later came to bilateral sympathectomy, left-sided sympathectomy produced vasodilatation on the left, without any effects on the right, just as would normally be expected. Excision or accurate alcohol block of the second and third ganglions produces satisfactory vasodila-

separated from the tips of the fingers, leaving new pink, healthy skin beneath by the end of ten to fourteen days. No painful or vasospastic sequelae had developed at the end of six months. One patient was subsequently subjected to prolonged immersion

after the second exposure this finger contracted, became atrophic and useless and had to be amputated.

I have not employed sympathetic block or ganglionectomy in acute stages of immersion foot. As

TABLE 1 Summary of Data on Patients with Immersion Foot *

CASE No	NATURE OF EXPOSURE	DEGREE	DURATION OF SYMPTOMS ON ADMISSION	SYMPTOMS	TREATMENT	RESULT
1	8 days in open dory off Grand Banks (2/40)	2nd	Immediate	Hyperemia, acute pain ulceration of digits	Physiotherapy†	Returned to work after year had some deep pain
2	4 days on raft in Arctic waters (1/41)	3rd	1 mo	Gangrene of hands and feet	Amputation of hands and feet	
3	3 days on raft above Arctic Circle	3rd (hands and feet); 2nd (knees)	6 mo	Gangrene of hands and feet, ulcerations over knees	Amputation of feet and fingers; procaine lumbar sympathetic blocks	Knee lesions healed quickly
4	11½ days in boat in North Atlantic (12/42)	2nd	1 mo	Anesthesia +, deep pain in ankles and feet + + + +	Alcohol lumbar sympathetic block	Anesthesia relieved, pain unrelieved, spontaneous improvement after 14 mo
5	1½ hr on driftwood in North Atlantic (2/42)	1st	5 mo	Only right foot affected hyperesthesia +, hyperhidrosis +, cyanotic attacks + +, pain +	Sympathectomy (right)	Apparently relieved of all symptoms returned to sea duty
6	16 days in open boat in Arctic waters (12/42)	2nd	2 mo	Anesthesia + + + + hyperesthesia + + + + hyperhidrosis + + + + cold intolerance + +, deep pain + + + +	Physiotherapy	Picture unchanged 6 mo after treatment
7	4 days in boat in North Atlantic (1/43)	2nd	4 mo	Anesthesia + + hyperesthesia + + cyanotic attacks + +, pain + + + +	Alcohol lumbar sympathetic blocks	Relieved of all symptoms except pain, rehabilitated to sedentary task after 1 yr
8	4 days in boat in North Atlantic (1/43)	2nd	10 mo	Anesthesia + + hyperesthesia + + hyperhidrosis + + cyanotic attacks + pain + + + +	Alcohol lumbar sympathetic blocks sympathectomy	Relieved of all symptoms except pain has been disabled 2½ yr
9	9 days in open boat in North Atlantic (9/42)	2nd	9 mo	Anesthesia + + + + hyperhidrosis + + + +, intolerance to cold + + + + cyanotic attacks +, deep pain + + + +	Alcohol lumbar sympathetic blocks physiotherapy	Relieved of anesthesia and hyperhidrosis cold tolerance improved pain unrelieved still disabled
10	12 days in open boat in North Atlantic (6/43)	2nd	6 mo	Hyperhidrosis + + + + deep pain + + + +	Physiotherapy	Unimproved after 6 wk, could not be followed.
11	Several hours in water, 3 days in boat (1/43)	2nd	6 mo	Anesthesia + +, claudication + + +, little deep pain	Sympathectomy	Apparently cured returned to duty
12	8 days in open boat in North Atlantic (1/42)	2nd	12 mo	Anesthesia +, hyperesthesia + + +, cyanotic attacks + + pain + + + +	Alcohol lumbar sympathetic blocks	Relieved of cutaneous symptoms cyanosis diminished pain unrelieved
13	10 days in open boat in North Atlantic (winter of 1917) fractured foot in 1944	2nd	27 yr	Anesthesia of soles, trophic ulcer of sole	Alcohol lumbar sympathetic blocks	Unimproved
14	3 hr in open boat in North Atlantic (4/44)	1st	6 wk.	Anesthesia + + + + deep pain + +	Physiotherapy†	Anesthesia remains on soles of feet returned to duty 8/44 still has pain
15	19 days in open boat in Indian Ocean (6/42)	2nd	16 mo	Intolerance to cold + + + + hyperhidrosis + + + + deep pain + + + +	Alcohol lumbar sympathetic blocks	Improved tolerance to cold hyperhidrosis relieved pain unaffected still disabled
16	3 hr on driftwood in North Sea (2/45)	1st	6 wk	Hyperhidrosis + + + + claudication + + +	Alcohol lumbar sympathetic blocks	Apparently cured

*Fifteen patients seen for other conditions gave histories suggesting first-degree immersion foot, with complete recovery within two to six weeks, 7 patients seen for other conditions gave histories suggesting second-degree immersion foot, with complete recovery within six weeks to three months.

†Physiotherapy included cooling, vascular exercises, paves, infra red rays, and whirlpool as indicated.

in comparatively warm water when his ship was torpedoed in the Pacific. Although he did not develop acute symptoms, within six weeks after the second exposure atrophy and thinning of the skin of a little finger appeared. Within three months

White² has pointed out, in the acute stage there is evidence of sympathetic-nerve damage — and presumably local sympathetic denervation of the vessels — in the absence of sweating, hyperemia is already present. For treatment of certain of the

quelae of frostbite or immersion foot, however, sympathetic-nerve block or ganglionectomy appears to be indicated. The clinical features of the cases on which this assumption is based are summarized in the accompanying tables.

It is a singular fact that the disturbances of cutaneous sensitivity are almost invariably removed by sympathectomy. In some patients a temporary sympathetic block not involving the autonomic nerves immediately restores cutaneous sensitivity and relieves hyperesthesia. In others there is a return to normal within two or three days after ganglion block by alcohol injection or ganglionectomy, but it should be noted, as already stated, that these symptoms do not usually contribute much to permanent disability. One would hesi-

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1	In air temperature of 10°F for 8 hr (1938)	3rd (8 fingers)	7 yr	Stiffness and pain in hands on exposure to cold	Repeated procaine blocks (previous treatment had included amputation and grafts)	No improvement
2	Worked all day standing on ice (1933)	2nd (both feet)	9 yr	Vasospasm and ulceration of toes, trophic ulcer of sole	Sympathectomy	Toes healed, trophic ulcer remained.
3	3 days in air temperature of 20-30°F (1943)	1st (4 fingers)	Immediate	Dry gangrene of fingertips hyperhidrosis++++	Repeated procaine blocks	Apparently cured returned to duty after 6 wk. re-exposure caused contracture of little finger
4	3 days in air temperature of 20-30°F (1943)	1st (2 fingers)	Immediate	Dry gangrene of fingertips hyperhidrosis++++ hyperesthesia+	Repeated procaine blocks	Apparently cured in 8 wk
5	3 days in air temperature of 20-30°F (1943)	1st (6 fingers)	Immediate	Dry gangrene of fingertips hyperhidrosis++ anes-thesia in fingers++	Repeated procaine blocks	Apparently cured
6	Shoveled for 3 hr at temperature of 20°F	2d (2 fingers)	Immediate	Acute swelling of hand ulceration of 2 fingers	Physiotherapy	Amputation of tips of fingers moderate stiffness of fingers.
7	Worked for 4 hr on metal parts in air temperature of 30°F (12/42)	2nd (1 finger)	10 mo	Intolerance to cold++++ chronic fissures and ulceration stiffness of distal joint	Alcohol sympathetic blocks	Ulcer healed but pain remained end of finger amputated with cure

tate to recommend bilateral ganglionectomy for relief of these symptoms alone. If a block lasting six to eight months can be performed by alcohol injection, it is worth while. Recurrence of sympathetic activity is not associated with return of these symptoms. If the symptoms are particularly distressing and if it is impossible to obtain satisfactory alcohol block, as it is in some cases, sympathectomy is justified.

If persistent and annoying symptoms of circulatory insufficiency resembling vasospasm are present, sympathectomy is helpful. If excessive sweating, Raynaud's phenomenon or intermittent claudication is prominent in the clinical picture, sympathectomy results in marked improvement. Since these symptoms tend to regress spontaneously, the decision to perform sympathectomy may be safely postponed. If thinning of the skin appears within the first three months, sympathectomy should be

and the lumbar and perhaps the sacral segments. Extirpation of the first, second and third lumbar ganglia produces satisfactory sympathetic denervation in the lower extremity. There are interlacing fibers on the anterior surfaces of the bodies of the lumbar vertebrae, and a few patients seem to have some crossing of innervation, at least paravertebral blocks of the second and third ganglia of one side—using 2 cc of 2 per cent procaine to each ganglion, amounts presumably not large enough to diffuse to the opposite side—sometimes produce vasodilator effects on the opposite side. In one patient, however, in whom this effect was constant on several occasions and who later came to bilateral sympathectomy, left-sided sympathectomy produced vasodilatation on the left, without any effects on the right, just as would normally be expected. Excision or accurate alcohol block of the second and third ganglia produces satisfactory vasodila-

tation in the leg and foot, although in some cases the effect seems to be enhanced by additional block of the first lumbar ganglion. An effort should be made to spare one first lumbar ganglion — at least when doing alcohol block — to avoid disturbances of ejaculatory power. Although it is convenient to speak of the ganglions in respect to the vertebral bodies on which they rest, there is actually variation in the size, shape and number of these structures

unless an otherwise unnecessary wide dissection is performed. This may in some measure be overcome by use of a preliminary film marking the location of the umbilicus, as shown in Figure 1. For an obese patient or a case in which high spinal anesthesia is not available, the lumbar approach to the sympathetic ganglions is preferable.

For lumbar sympathetic block with alcohol, the patient is placed in the prone position with the



FIGURE 1 *An Aid to Identification of the Lumbar Vertebrae for Sympathectomy by the Retroperitoneal Abdominal Approach*

A metal marker in the umbilicus is projected truly perpendicularly to determine the plane in which the umbilicus lies with reference to the vertebral bodies

These variations account for the difficulty in some cases of obtaining satisfactory sympathectomy by the blind procedure of alcohol block.

In the average patient, lumbar sympathectomy is accomplished by use of the Flothow approach, which is described elsewhere.¹³ A possible disadvantage of this method is compared with the method described by the Pacini, that it is sometimes difficult to locate the second exposure atrophy given vertebral body skin of a little finger appeared

spine flexed as well as possible by pillows beneath the abdomen. A preliminary intravenous injection of 11 to 16 mg of morphine is of value. The spinous processes are counted from the fourth interspace, which lies opposite the iliac crests, and checked by counting from above downward, beginning with the twelfth rib and tracing its course to locate the twelfth thoracic spine. Wheals are made from three to four fingerbreadths lateral to the superior faces of the second and third spinous

processes. A 12.5-cm, 22-gauge, blunt-bevel spinal needle is inserted through the upper wheal and advanced inward and slightly medially to touch the side of the body of the vertebra. If it touches the transverse process instead, it is withdrawn, angled slightly cephalad in addition to its medial angulation and pushed inward until the body of the vertebra is reached. The needle is turned until the bevel faces the body of the vertebra, and the point is slid down the lateral face of the vertebral body until it is felt to pass the anterolateral "corner" of the body. The stylet is removed, and aspiration is done. A second needle is inserted in the same way to the third lumbar ganglion. In this situation the point of the needle may easily enter the vena cava or aorta, but no harm is done if it is slightly withdrawn, to remove the bevel to a more superficial level before injecting. When blocking the ganglions in the lumbar region, there is little fear of making an accidental subarachnoid injection, since the sympathetic trunk and ganglions lie quite deep relative to the somatic nerves and intervertebral foramina. When the point is properly situated, 2 cc. of 2 per cent solution of Metycaine Hydrochloride or procaine is injected through each needle and the effect on the feet is observed.

If this small amount of anesthetic solution quickly produces vasodilatation, accurate location of the needles in or near one or more of the ganglions is indicated. Four cubic centimeters of absolute alcohol is then injected through each needle. This causes an immediate burning pain in the back and may produce painful sensations in the abdomen, but these quickly disappear. Later there is stiffness of the back and dull pain, which should not last through the second day.

For successful treatment, alcohol neuritis of the somatic nerves must be avoided. This occurs when they are speared and alcohol works its way into the nerves or when small amounts of alcohol are injected about them. Even the largest somatic nerves may be injected with alcohol if a sufficient amount is used to produce degeneration, but small amounts serve to irritate them and produce neuritis, which may last for months.

Neuritis is avoided in the following way. First, no attempt should be made to inject the fourth and fifth lumbar ganglions with alcohol. Second, the needles should be inserted in such a way that they will not produce paresthesia down the extremity. This is done by using only a little local anesthetic solution in the muscle beneath the wheal and by injecting none deep to the transverse process until the ganglion has been reached. If any needle in traversing the back toward the body of the vertebra produces pain down the leg or in the hip or genitals, it should be withdrawn and inserted at a different level, usually opposite the center of the spinous process. With regard to paresthesia, insertion of the needle into one of the ganglions produces pain

radiating downward to the coccyx, and when this fortunate accident occurs, alcohol may be injected without delay.

The technic of temporary sympathetic block is much less exacting. The needles are inserted in the same manner, but more local anesthetic solution may be used on the way in to make the procedure less painful. When the needles are inserted in approximately the proper location, the area should be flooded with 5 to 10 cc. of 1 per cent solution of Metycaine Hydrochloride or procaine through each needle. This almost always results in sympathetic block. Or temporary block may be done more easily with a caudal or peridural injection.^{14, 15}

Thoracic Sympathectomy and Block

It is much more difficult to produce permanent sympathetic denervation in the upper extremity than in the lower. The operation of Smithwick,¹⁶ however, seems to have largely overcome the defects of this procedure. The indications for operative sympathectomy in the upper extremity should be more demanding than for that in the lower, since the operation is somewhat more exacting and difficult than lumbar sympathectomy and at the same time is often less satisfactory.

For diagnostic or therapeutic block of the sympathetic supply to the upper extremity, the first and second thoracic sympathetic ganglions are anesthetized. The patient is placed in the lateral or prone position, and the thoracic and cervical spine is flexed. A wheal is made two fingerbreadths lateral to the spine of the seventh cervical vertebra, and the muscle tissue is anesthetized down to the transverse process of the first thoracic vertebra. From an angle of about 10°, a 22-gauge blunt-bevel spinal or nerve-block needle is inserted through the wheal down to the transverse process of the first thoracic vertebra. The bevel is worked over the transverse process until it drops across its inferior border, and its course is continued inward and slightly medially until the lateral aspect of the body of the vertebra is reached. For diagnostic or temporary therapeutic block, 5 cc. of a 2 per cent solution of procaine should be injected. The same procedure is carried out from a wheal opposite the spinous process of the first thoracic vertebra to block the second thoracic ganglion. Should bone bar the needle's progress 0.5 cc. or less beneath the transverse process, the posterior surface of the body of the vertebra in the region of the intervertebral foramen has been touched, and the needle should be withdrawn and reinserted from a wheal made slightly more lateral. Aspiration should precede injection to avoid subarachnoid injection. Neither procaine nor alcohol should be injected intraneurally into a somatic nerve near the spine, since it is said to be possible to damage the spinal cord by solution forced into it along the nerve.¹⁷

tation in the leg and foot, although in some cases the effect seems to be enhanced by additional block of the first lumbar ganglion. An effort should be made to spare one first lumbar ganglion — at least when doing alcohol block — to avoid disturbances of ejaculatory power. Although it is convenient to speak of the ganglions in respect to the vertebral bodies on which they rest, there is actually variation in the size, shape and number of these structures

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PENICILLIN IN THE TREATMENT OF TETANUS*

Report of Two Cases

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BOSTON

TETANUS is an extremely serious disease, whose mortality rate remains extremely high in spite of the institution of heroic measures for combating the intoxication and controlling the convulsive seizures that it produces. Treatment of this infection necessitates the careful control of at least five factors if a successful outcome is to be expected. Often, even with the most rigid adherence to these principles, failure results.

Of the greatest importance is the rapid and effective neutralization of absorbed tetanus toxin. If this has already been fixed to nervous tissue, it apparently cannot be inactivated by antitoxin, regardless of how large a quantity is given. The sole effect of the administration of antiserum therefore appears to be the neutralization of toxic material still circulating in the blood stream and the maintenance of an antitoxic level sufficiently high to overcome the effect of any additional tetanospasmin that may be absorbed from the local focus of infection. The antitoxic serum must be administered initially in large amounts and repeated at frequent intervals for several days to a week or more. An adequate procedure is the injection of 50,000 American units intravenously, 50,000 units intramuscularly and 10,000 to 20,000 units subcutaneously around the local wound, if one is present. Ten thousand units should be given every twenty-four hours thereafter until the condition of the patient warrants cessation of antitoxic therapy.

All patients with tetanus have muscle spasm ranging in severity from that involving only the tissue immediately surrounding the site of injury (local tetanus) to that in which severe, generalized tonic convulsions are initiated by the slightest stimulus. A great variety of drugs have been employed to relieve spasm and convulsions, and almost everyone who has treated tetanus has his favorite. Thus, magnesium sulfate, morphine, avertin, paraldehyde, sodium luminal and inhalation anesthesia have all been used. Each of these agents has its proponents, but it appears that any agent is adequate that is capable of exerting a strong anticonvulsive effect with minimal danger from the necessarily large and frequent doses. Any of these sedative drugs must be given in large enough amounts and frequently enough to induce complete and prolonged relaxation. Careful watch must be kept for signs of overdosage.

Many patients with tetanus are unable to take food because of inability to open the mouth owing to spasm of the jaw muscles or because attempts at eating initiate convulsive spasms. For this reason, it is often impossible to maintain a normal state of nutrition by means of the oral route, rendering it essential that adequate calories and vitamins be administered, at first parenterally and then by means of gavage, until the patient can take food by mouth without discomfort. The plasma protein may fall to low levels because of inadequate food intake, and a close check should be kept on it.

Rigid attention must be paid to the fluid and electrolyte balance in tetanus patients, because they cannot take water by mouth and may lose fluid and salts with extreme rapidity as a result of the sweating and fever that accompany the convulsive seizures. Consequently, 5 per cent glucose in water or physiologic sodium chloride solution should be given parenterally in adequate quantities. The

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For alcohol block in the thoracic ganglions, the same procedure is adopted as before, but the preliminary solution superficial to the transverse process is injected sparingly. When the needles seem properly placed in the region of the ganglion on the lateral aspects of the bodies of the vertebrae, 2 cc of a 2 per cent solution of procaine is injected through each needle and the effect is observed. If prompt vasodilatation occurs from such a small amount of procaine, the needle is situated in or very near the desired location. Four cubic centimeters of absolute alcohol is injected through each needle, which is then withdrawn and inserted to the posterior surface of the body of the vertebra near the intervertebral foramen above the ganglion injected. Aspiration with a dry syringe should be done, making sure that no spinal fluid appears. In these positions an additional 1 cc of absolute alcohol should be injected through each needle to block the first and second thoracic somatic nerves.

The somatic nerves are deliberately blocked in this instance with sufficient alcohol to produce at least partial degeneration. This is done to prevent painful neuritis, since in the thoracic region it is practically impossible to inject the sympathetic ganglions without affecting the intercostal nerves. Although intercostal neuritis is seldom so severe as lumbar plexus neuritis, it is to be avoided. No disturbance of function seems to result from this procedure, despite the fact that the first thoracic nerve contributes to the brachial plexus. Somatic anesthesia thus produced lasts scarcely a month, although a proper sympathetic block lasts for six to eight months.

Additional dangers of thoracic injection are present that are not encountered in the lumbar region. There is always the possibility of spinal anesthesia from injecting into an intervertebral foramen or into an extra long dural sleeve. As was described above, careful aspiration with a dry syringe before injection should serve to prevent this accident. The injection is begun rather closer to the midline than it is in the lumbar region to avoid entering the pleura, since if this is pierced, together with the lung, painful apical pneumothorax may result, but this is not dangerous unless the patient is emphysematous. If the needle is not inserted along the bony landmark, it may go astray and pierce the esophagus, but this does no harm. I have not pierced a large vessel in doing this injection, but it might happen. So long as an anesthetic solution is not injected intravascularly, no harm will result.

It should not be concluded from the relative space devoted to alcohol block and ganglionectomy that the former procedure is always the technic of choice for producing sympathetic denervation. Ganglionectomy is the more exact and often the more satisfactory method. It is hoped that the block

technics herein described will be of assistance to others in avoiding alcohol neuritis.

EVALUATION OF DISABILITY

In evaluating disability as a result of frostbite and immersion foot, it should be borne in mind that in first- and second-degree cases the changes may not become static until eighteen months after injury. In third-degree cases the diseased parts are usually amputated, so that earlier evaluation is often possible. In examination of patients of the first two types, particular attention should be paid to the amount of pain in the feet from walking and pain in the hand from working. If a history is spontaneously given of deep-seated aching pain "in the bones," it is usually valid. The amount of disturbance of pliability of the structures should be estimated. The condition of the skin with regard to atrophy should be noted, together with evidence of circulatory insufficiency. Most patients presenting vasospastic signs have not reached the maximum benefit of medical treatment. Circulatory disturbance with the skin already thinning represents a real danger of future contracture or ulceration.

Many patients with first-degree frostbite or immersion foot completely recover. In frostbite of the fingers particularly, the disability may be limited to one finger. About half the patients with second-degree immersion foot showing late sequelae remain disabled for work involving prolonged standing or walking. Many of them cannot work under all weather conditions, patients with frostbite of the fingers usually cannot do manual labor in cold weather, and some, depending on the number of fingers affected and the extent of deep-seated pain, cannot perform skilled manual labor.

The problem of rehabilitation of disabled sufferers from immersion foot or frostbite involves knowledge in many fields, but the medical facts, especially those with reference to pain, stamina and effects of climate, should be scrupulously regarded.

SUMMARY

Careful study of a small group of patients with immersion foot or frostbite indicates that sympathetic denervation produces beneficial effects on certain late symptoms but does not always prevent partial disability. It is probable that similar results can be obtained in cases of trench foot showing similar lesions.

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lowing the administration of the original dose. The muscle spasm gradually relaxed, the pain in the abdomen diminished slowly, and 8 days after admission the patient was sleeping comfortably without sedation and complained very little of muscle spasm anywhere. The wound in the hand healed well without grafting and was completely closed 4 weeks after excision.

On the 19th day, the patient complained of numbness and severe pain in the left lower extremity. Examination showed the entire leg to be swollen and tense, it was mottled purplish gray, and the superficial saphenous vein could be palpated as a firm structure for almost its entire course in the thigh. There was tenderness to palpation in the inguinal region but not over the saphenous vein, and marked calf tenderness on the left. Homans' sign was absent. The arterial pulsations in both legs were within normal limits. At that time the temperature rose to 106°F and remained between 99 and 100°F for the next 8 days, after which it returned to normal for the remainder of the hospital stay. A diagnosis of left femoral and iliac thrombophlebitis with moderate vasospasm was made, and treatment by hot moist packs and papaverine, 30 mg every 6 hours, was instituted. Severe pain in the left thigh and tenderness of the calf and upper leg persisted for 5 days, after which they diminished. The swelling and tenderness of the leg gradually decreased, but these were still present to a moderate degree when the patient was discharged 45 days after admission.

A gram stain of smears made directly from the wound at the time of admission showed no organisms that could be recognized as the tetanus bacillus. Cultures of the hand made at the same time revealed vegetative and spore forms of *C. tetani* in large numbers. Subsequent bacteriologic examination of the wound on the hand was carried out every 12 hours for the first 4 days and every 24 hours thereafter for the next week. Twenty-four hours after treatment with antitoxin, surgery and penicillin had been instituted, the anaerobic organism could not be demonstrated in the wound, and it was not recovered in any of the later cultures.

Laboratory examinations made during the course of the illness revealed urines that were always within normal limits. The white-cell count, which, as previously stated, had been 10,000 on admission, fell to 2000, with 42 per cent neutrophils and 58 per cent lymphocytes, 2 hours after the administration of the tetanus antitoxin. Eight hours later, it had risen to 21,000, with 89 per cent neutrophils, and for the next 3 days it ranged between this level and 34,600. Thereafter it returned to within normal limits until the episode of thrombophlebitis, when it again rose, to 17,650, with 80 per cent neutrophils, it then declined gradually and at the time of discharge was 7750, with a normal differential count. The hemoglobin ranged between 12 and 15 gm. The nonprotein nitrogen varied from 33 to 35 mg per 100 cc. and the serum protein from 5.7 to 6.1 gm, with 3.5 to 3.6 gm of albumin per 100 cc. The plasma chloride level was 94.3 milliequivalents per liter. An electrocardiogram taken 3 days after admission was within normal limits.

CASE 2 R. P., a 4-year-old Negro, was admitted to the Haynes Memorial Hospital with a diagnosis of tetanus. The family and past histories were irrelevant. The illness began 10 days prior to admission, when the patient's mother noticed a cut on his finger. No attention was paid to this, and he got along well until the morning of entry to the hospital, when it was noted that he could not stand up. A physician discovered severe trismus and muscle spasm and sent the patient to the hospital.

On admission, the temperature was 99.4°F, the pulse 84, and the respirations 26. Physical examination revealed a well developed, thin boy who appeared acutely ill. He was in marked opisthotonos, with the back sharply hyperextended and both feet extended in the equinus position. The skin was flushed, and the veins of the head were engorged. Examination of the head was essentially negative. There was marked rigidity of the neck. The pupils were small, round and equal and reacted to light and accommodation. The teeth were clenched tightly, but the patient could open his mouth voluntarily about 1 cm. to permit passage of a glass drinking straw. The lungs were clear to percussion and auscultation. The heart was not enlarged, the sounds were of good quality, there was sinus arrhythmia with a tachycardia, and no murmurs were heard. The pulmonary second sound was greater than the aortic. The blood pressure was

150/84. Examination of the abdomen revealed marked spasm of all the muscles and hyperactive but equal reflexes. The genitalia were within normal limits. All the extremities were in marked spasm and could not be extended or flexed except with great difficulty. On the medial aspect of the left malleolus there was a deep wound 1 cm. in length, covered with purulent exudate. Over the lateral aspect of the right heel there was a ruptured vesicle that did not appear to be infected. The skin over the terminal phalanges of the 2nd, 3rd, 4th and 5th toes of the right foot was lacerated in numerous places, but no signs of infection were present. One third of the nail of the 4th finger of the left hand was easily removed and revealed thin, greenish-yellow, foul-smelling pus, the eponychium was red and swollen.

Immediately after admission the patient was given 40,000 units of tetanus antitoxin intravenously, 30,000 units intramuscularly, 10,000 subcutaneously about the wound on the 4th finger of the left hand and 10,000 units under the skin around the lesion on the medial aspect of the left foot. Sodium luminal (0.13 gm) was given parenterally as often as required to keep the patient at rest. Physiologic saline solution was administered subcutaneously. Penicillin was given in a dosage of 10,000 units every hour by constant intramuscular drip and continued for 11 days. Shortly after injection of the horse serum the patient had several convulsions but these were controlled by sodium luminal. A generalized urticarial rash appeared 30 minutes after giving the antitoxin, but disappeared after the administration of 0.25 cc of a 1:1000 solution of epinephrine given every 15 minutes for 1 hour.

The terminal phalanx of the 4th finger of the left hand was amputated and the wound on the left ankle was incised and drained. More extensive surgery for removal of all the infected tissue could not be carried out because of the mutilation that would have resulted. Convulsions occurred frequently even with large doses of sodium luminal and paraldehyde injected rectally as an adjunct to the barbiturate therapy. Fifteen hundred units of tetanus antitoxin were given every 24 hours for 2 days and then increased to 10,000 units daily for 7 days. On the 3rd day, an attempt to pass a tube through the nose resulted in profuse bleeding from both nostrils and the mouth, and no further attempt was made until the 7th day, when a tube was successfully passed and frequent feeding was instituted. For the first week fluid and electrolyte balances were maintained by the subcutaneous and intravenous administration of glucose, salt and vitamins. On the 5th day, the patient had numerous convulsions, only partially controlled by sodium luminal and paraldehyde. The use of both these drugs was stopped and magnesium sulfate was administered intramuscularly. This agent controlled the convulsions well until the 8th day, when it was discontinued because it was thought to have produced respiratory arrest. The convulsive seizures were easily controlled thereafter with moderate doses of sodium luminal and paraldehyde, administered parenterally.

On the 8th day, there appeared to be some relaxation of the muscles of the jaws. On the 10th, 11th, 12th and 16th days the patient had sudden severe tonic spasms during which respirations ceased and he became markedly cyanotic for 1 to 1½ minutes. Artificial respiration was extremely difficult because of the boardlike rigidity of the chest and abdominal muscles during these seizures and breathing was apparently resumed spontaneously. The temperature, which had been only slightly elevated, rose to 105°F on the 10th day, but fell rapidly so that it was within normal limits within 24 hours, it remained so during the remainder of the hospital stay. After the 16th day, the patient began to improve markedly gradually required less sedative drugs and lost the muscle spasm. At the end of 3 weeks in the hospital, sedation was no longer necessary, increased muscle tonus had almost completely disappeared, and the patient was taking food by mouth. He was kept in the hospital for another 5 weeks to regain his strength and weight, and 59 days after admission he was discharged to the care of a physiotherapist because of residual weakness and slight difficulty in walking.

During the illness the white-cell count ranged from 10,250 on admission to 24,900 on one occasion, with an average of 16,000, the differential count was always within normal limits. The urine showed no abnormalities on numerous examinations. The hemoglobin varied between 7 and 10.5 gm. The nonprotein nitrogen was 25 mg per 100 cc. The plasma

blood chloride and nonprotein nitrogen levels should be frequently determined

Since the toxin that is responsible for all the symptoms is formed by *Clostridium tetani*, which has invaded and propagated in an area of injury, it is imperative that this focus of infection be removed to stop the further production and absorption of toxin. At present, the method of accomplishing this is surgical extirpation of the wound with a wide margin of healthy tissue around it and subsequent treatment with an oxidizing agent, such as activated zinc peroxide. This procedure is adopted when a single lesion is present. It may not be practical or even possible in certain cases with multiple lesions in those in which surgical removal of the local lesion would be seriously mutilating and in those in which no localized focus of infection can be discovered.

Penicillin has been shown by Herrell, Nichols and Heilman¹ to be active against *Cl. tetani* in vitro. The administration of this antibiotic agent to patients with tetanus infection and intoxication should therefore be a highly valuable aid to surgical measures, in eliminating whatever bacteria may remain after removal of a single lesion or in eradicating organisms that cannot be reached by surgery. Reports of the use of penicillin in the treatment of tetanus are rare. Buxton and Kurman² have described 2 patients with tetanus both of whom recovered after treatment with large doses of penicillin and antitoxin.

The purpose of administering penicillin in the 2 cases described below was to determine the efficacy of the antibiotic substance in eliminating tetanus bacilli from wounds, and to ascertain whether the administration of this agent had a favorable effect on the course of the disease.

CASE REPORTS

CASE 1 W. B., a 30-year-old man, was admitted to the hospital with a chief complaint of pain and stiffness of the right jaw of 3 days' duration. The family history was irrelevant. The patient had been rejected by Selective Service because of asthma and bronchitis.

Two weeks prior to entry to the hospital, while repairing a tire on his automobile, the patient received a large, triangular-shaped laceration on the dorsum of the left hand when the car slipped off of the jack. He was seen within a short time by a physician, who, after cleaning and irrigating the wound, dusted sulfanilamide powder into it. During the next 10 days, the injured area was again cleaned and treated with sulfanilamide powder and appeared to be healing well. Seventy-two hours before admission, pain and stiffness of the right jaw, most marked when chewing and absent when not eating, was noted. This persisted but did not increase in severity. Two days after the onset of these symptoms, the patient again consulted his physician. Examination at that time revealed some stiffness of the right mandible but no marked trismus. Since no antitoxin had been given following the hand injury, the possibility of tetanus was considered and the patient was referred to the Haynes Memorial Hospital. There was no history of headache, stiffness of the back or neck or localized spasm of the arm or hand around the wound.

Physical examination on admission revealed a well nourished, well developed man who appeared quite healthy. The

temperature was 98.6°F, the pulse 68, and the respirations 18. There was a triangular laceration 8 cm in its longest diameter, crusted with dried sulfanilamide powder, on the dorsum of the left hand. The skin around the wound appeared normal in color and was not swollen or tender. There was no cervical, axillary, epitrochlear or inguinal lymphadenopathy. Examination of the head was essentially negative, and the neck could be flexed anteriorly and laterally with great ease. The pupils were round and equal, and reacted to light and on accommodation. The extraocular movements were within normal limits. Examination of the eyegrounds revealed no abnormalities. The patient was unable to open the mouth widely because of pain at the angle of the right mandible. Palpation of the masseters revealed no spasm, but there was a point of tenderness 3 cm anterior to the angle of the right jaw. Examination of the teeth revealed swelling of the gums and tenderness over the lateral side of the lower right 3rd molar. The pharynx could not be well visualized because the mouth could not be opened beyond 2 fingerbreadths. The lungs were clear to percussion and auscultation. The heart was not enlarged, and the sounds were of good quality, the rhythm was regular, and no rubs or murmurs could be detected. The aortic second sound was louder than the pulmonic. The blood pressure was 118/70. The abdomen was soft, with no demonstrable tenderness, spasm or hernias. The liver, spleen and kidneys were not palpable. The genitalia were within normal limits. All the muscles were strong, and no evidence of spasm was found. There was no limitation of motion of any of the joints. All the deep and superficial reflexes were present, equal and of normal activity. The cranial nerves were intact. Kernig's and Chvostek's signs were negative. The patient was mentally alert and extremely responsive.

Laboratory examinations on admission revealed no albumin, sugar, ketone or abnormal cellular elements in the urine, which had a specific gravity of 1.018. The hemoglobin was 15 gm. The white-cell count was 10,000, with 70 per cent neutrophils, 26 per cent lymphocytes, 2 per cent monocytes and 2 per cent eosinophils.

Because of the demonstration of localized disease over the 3rd right molar, which might account for the slight trismus and the absence of any other signs of tetanus, it was decided to withhold antitoxin. The history of asthma contributed to this decision, although endermal and conjunctival tests with horse serum gave no reactions.

Ten hours after admission, the patient complained of cramping, generalized abdominal pain, coming on for short periods of time, and a "crushing feeling" over the precordium, radiating straight through to the back. These symptoms were accompanied by a sensation of suffocation. Examination revealed slight stiffness of the back, moderate spasm of the abdominal muscles and the same degree of trismus as had been noted on admission.

Because the development of the abdominal muscle spasm was thought to be due to the action of tetanus toxin, tetanus antitoxin was administered in the following manner: 50,000 units was given intravenously, 50,000 intramuscularly and 10,000 subcutaneously around the wound on the dorsum of the hand. At the same time a regimen of 15,000 units of penicillin every 3 hours and paraldehyde intramuscularly varying in amounts from 20 to 60 cc a day was instituted. The surgical consultant who excised the hand wound found boardlike rigidity of the abdomen 4 hours after the onset of pain and suggested the possibility of a ruptured viscus, particularly since x-ray examination revealed obliteration of the left psoas shadow. An exploratory laparotomy was therefore performed, but no intra-abdominal disease was found. Postoperatively, Wangensteen suction was maintained for 48 hours. A lumbar puncture carried out prior to operation revealed no abnormality of the spinal fluid. The temperature ranged between 101 and 103°F for the first 6 postoperative days and then returned to normal.

During the next few days, 10 cc of paraldehyde was administered intramuscularly every 4 hours, and this maintained the patient at practically continuous rest. Penicillin was continued for 12 days at a rate of 160,000 units a day. The Kernig reaction gradually became positive. Marked spasm of the abdominal and back muscles persisted accompanied by pain, of which the patient complained bitterly. There was also rigidity of the neck and a moderate degree of trismus. Ten thousand units of tetanus antitoxin were given intramuscularly every 24 hours for 6 days fol-

belief that the disturbance is due solely to vitamin lack. White,⁹ on the other hand, classified diabetic neuritis in children under the heading of deficiencies.

Jolliffe, McLester and Sherman,¹⁰ in discussing the prevalence of various types of nutritional polyneuropathy in diabetic and alcoholic patients, suggested that thiamine deficiency might account wholly or in part for such disorders as characteristic bilateral symmetrical polyneuropathy, combined system disease, Wernicke's syndrome and certain organic reaction psychoses.

Meiklejohn¹¹ questioned the characterization of thiamine as the so-called "antineuritic vitamin." He pointed out that although thiamine therapy remedied the functional metabolic disturbance of nerve tissue produced by lack of this substance, the exact relation of thiamine to the organic changes of polyneuritis was still unknown.

The early experimental work in the production of polyneuropathy in animals by induced thiamine deficiency was extremely disappointing. Moreover, polyneuropathy could be produced in different species of animals by diets deficient in riboflavin, pyridoxin and panthothenic acid only, and could be cured by the administration of these components of the vitamin B complex.¹² This suggested that various species of animals might react differently to deficiency of the various components of the vitamin B complex.

Street¹³ found that a diet deficient in thiamine produced irreversible neurologic changes in dogs. He had maintained the animals on a partially thiamine-deficient diet until signs of peripheral neuritis developed. Large doses of thiamine chloride given during the following month had no therapeutic effect, and histologic examination revealed degeneration of the peripheral nerves, anterior horns and posterior columns of the cord.

Swank and Bessey¹⁴ observed in pigeons, and Leblond and Chaulin-Serviniere¹⁵ in monkeys, that the nature and extent of neurologic changes depended on the degree and duration of the vitamin deficiency. Severe or total deprivation of thiamine caused rapid prostration and death, without neurologic signs or pathologic changes in the nervous system. With partial restriction of thiamine over a considerable period of time, it was possible to produce definite signs and histologic evidence of polyneuropathy.

Needles¹⁶ found no history of deficient intake of thiamine in his patients with diabetic neuropathy. He¹⁷ treated 7 patients with advanced neuropathy with thiamine chloride and observed no objective improvement in 4. He believed that the pathologic changes in these patients were irreversible. On the other hand, Fein, Ralli and Jolliffe¹⁸ administered thiamine by mouth to 9 diabetic patients with symmetrical peripheral polyneuropathy and observed complete recovery in 8 and some improvement in 1. Joslin, Root and Bailey¹⁹ believed that the improve-

ment in these cases was related not only to the thiamine administered but also to simultaneous regulation of the diabetes.

Williams and his co-workers^{20, 21} made observations in man similar to those made by others¹³⁻¹⁵ in animals. They found that prolonged *partial* restriction of thiamine produced neurologic disturbances such as weakness and paralysis of the thigh muscles and diminished vibratory sensation. The ankle jerks and knee jerks first became hyperactive, later diminished and finally disappeared. Early in the experiment, the subjects developed weakness, anorexia, nausea, epigastric distress and vomiting. Later there appeared marked weight loss, giddiness, apathy, confusion, inactivity and numbness, and tingling in the legs. The response of the neuropathy to thiamine therapy was extremely slow, and in 1 case the knee jerks and ankle jerks were still absent after four months of treatment. Williams concluded that polyneuropathy is a manifestation of advanced rather than of early thiamine deficiency.

Neuropathy in diabetic patients, however, is not the clear-cut syndrome that has been produced in animals and man by diets deficient in vitamins. In my experience it is frequently diffuse and disseminated and often presents a bizarre picture. The predominant manifestations may be of cerebral origin or be related to the spinal cord, or may be the result of changes in the peripheral nerves. Even neurologic syndromes, such as combined system disease or tabes, have been noted. Diabetic neuropathy also may simulate tumors or degenerative diseases of the nervous system or malignancy of the gastrointestinal tract.

In occasional patients the objective manifestations of the neuropathy are extremely marked when the subjective complaints are minimal. In most patients, however, the subjective manifestations of diabetic neuropathy develop first and may be present for a long time before definite neurologic signs can be elicited. In these the diagnosis of hysteria or psychoneurosis has frequently been considered before the true situation has been recognized.

Although diabetic neuropathy may involve any part of the nervous system, there is nevertheless a definite predilection for the peripheral nerves. This is of diagnostic significance in patients in whom other types of neurologic abnormality predominate, since the simultaneous existence of a peripheral neuritis makes the diagnosis of diabetic neuropathy likelier. It must be remembered, however, that in the diabetic patient the peripheral neuritis may be asymmetrical.²²

Also of diagnostic value is the fact that the spinal-fluid protein may be elevated in patients with minimal objective evidence of neuropathy. In other diabetic patients with signs of advanced neuropathy, however, the spinal-fluid protein is normal or only slightly elevated. A tabetic type of gold-sol curve has occasionally been observed.

protein level was 5.3 gm, with 3.6 gm of albumin per 100 cc. Gram stains of all the wounds revealed no tetanus bacilli, but these were obtained in culture from the wounds in the hand and foot. Cultures were made every 24 hours, but all were negative after penicillin therapy was instituted.

DISCUSSION

The favorable results obtained in these cases indicate that penicillin is a valuable adjuvant in the treatment of tetanus. The administration of large quantities of antitoxin and careful control of convulsions, as well as the maintenance of a good nutritive state and fluid balance, cannot be replaced by any antibacterial agent, regardless of its potency. Surgical removal of local areas of infection is important, but penicillin is probably a valuable aid in eliminating any organisms that are not removed by such a procedure. In cases of tetanus in which there are multiple lesions not all of which can be removed because of the resultant extensive mutilation, penicillin seems to be strongly indicated. Case 2 is a good example of such a situation. Penicillin appears to be of the greatest value in the cases of tetanus infection in which no localized area of bacterial invasion can be detected or in which it is impossible to eradicate the focus surgically.

SUMMARY AND CONCLUSIONS

Two cases of severe tetanus are reported in which recovery followed treatment with large amounts of antitoxin, surgical excision of the wounds and administration of large doses of penicillin.

Bacteriologic studies revealed that *Clostridium tetani* could no longer be isolated from the wounds in these patients twenty-four hours after the first administration of penicillin. The already demonstrated antibiotic influence of penicillin on this organism in vitro therefore appears to be confirmed in vivo.

The use of penicillin in tetanus appears to be most valuable in cases in which multiple lesions not all of which can be removed by surgical means are present or in which no focus of infection is detectable. This antibiotic agent is not intended to replace the administration of antitoxin, excision of wounds, adequate sedation and maintenance of a normal state of nutrition and hydration, but appears to be a highly important adjuvant to these other therapeutic measures.

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DIABETIC NEUROPATHY*

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THE frequency of neurologic abnormalities, particularly pain and paresthesias, in patients with diabetes mellitus prompted early observers to attribute the diabetes to a lesion of the nervous system. De Calvi¹ in 1864 was the first to consider that the diabetes might be the cause of the neurologic symptoms. Auché,² in a review of the literature published in 1890, stated that in diabetic patients all the nerves except those of the bladder and rectum could be involved. Woltman and Wilder³ in 1929 found only 42 reports, none of them between 1908 and 1928, of a pathologic examination of the spinal cord and peripheral nerves of diabetic patients. They examined the peripheral nerves of 10 such patients, in 3 of whom the spinal cord was also studied. In the single patient who had neurologic signs sufficient to justify a diagnosis of pseudo-tabes dorsalis, they found only a slight degeneration of the cord but marked changes in the peripheral nerves.

They ascribed diabetic neuropathy to arteriosclerotic changes in the vasa nervorum. Wagener, Dry and Wilder,⁴ confirming these findings, claimed that the neuritis, like diabetic retinitis, was due to some injury to the small venules and arterioles, but later Wilder⁵ admitted that he was not altogether satisfied with this explanation. In 1936, Jordan⁶ classified diabetic patients with neurologic symptoms in three groups, — hyperglycemic, circulatory or degenerative, and neuritic, — according to his concept of the probable etiology in each.

Cobb and Coggeshall⁷ included diabetes with pellagra, beriberi and cachexia as one of the deficiency and metabolic disorders capable of causing neuritis. Williams and Spies⁸ more specifically suggested that a deficiency in vitamin B₁ might be the cause of diabetic neuritis. Root⁹ believed that uncontrolled diabetes of long duration has some specific effect on nerve tissue, either by a direct metabolic influence or indirectly by means of a dietary deficiency. He admitted that thiamine may play a role in diabetic neuropathy, but contended that the rate of recovery after vitamin therapy is not always rapid or consistent enough to support the

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berg sign and absence of deep reflexes. The weight was only 48 pounds. Spinal-fluid examination was negative except for a total protein content of 78 mg per 100 cc.

Following discharge from the hospital the patient continued on a high-calorie, high-vitamin diet with yeast tablets and iron. The diabetes was controlled by diet and insulin. Six months after the development of the neuropathy, the gait was greatly improved and she was able to walk downstairs without support. The Romberg sign was negative, but the knee jerks were still absent. In the next 18 months she gained 37 pounds. Six years after the onset of the neuropathy, there were no neurologic symptoms except occasional cramps in the calves at night. Both knee jerks and the right ankle jerk had returned, and position sense had become normal. Vibration sense, however, was still impaired below the ankles — more on the right than on the left.

Comment: This patient developed symptoms and signs of severe peripheral neuropathy and of myelopathy immediately following the control of diabetic coma. The symptoms of myelopathy preceded the detection of objective abnormalities and disappeared before the latter cleared up. Almost complete recovery from both was noted 6 months after vitamin therapy was begun, and relatively normal health was maintained for 6 years.

CASE 5 D S (B I H 48219A), a 25-year-old man, was first seen in July, 1937, while in mild diabetic acidosis. The diabetes had been poorly controlled for 8 years. During the previous 6 months he had had intermittent swelling of the legs and fleeting pains in the legs and back. During the last 2 months he had had anorexia and nausea and had lost 25 pounds in weight. Examination disclosed diminished knee jerks, hyperesthesia of the lower extremities and tenderness of the calves.

During the next 2 months, while the diabetes was fairly well controlled, there gradually developed painful paresthesias in the chest, abdomen and arms in addition to those in the legs. Walking was difficult because of the paresthesias of the feet. Growing difficulty in controlling the diabetes led to the disclosure of pulmonary tuberculosis by x-ray examination. At this time the patient had hyperesthesia involving all the extremities and the trunk. There was hyperhidrosis below the level of the 12th dorsal segment. The left ankle jerk was absent, and the left knee jerk could be obtained only by reinforcement. The tongue was beefy and smooth. The spinal-fluid total protein was 90 mg per 100 cc, and the gold-sol curve was 2332211000.

During the next 3 weeks the patient received daily injections of 10 cc. of crude liver extract and 3.3 mg of thiamine chloride, together with 12 yeast tablets. The latter were soon omitted because of severe diarrhea. After transfer to a tubercular sanatorium, injection of thiamine chloride in doses of 6 mg were continued daily for a few weeks, the dosage was then decreased to 10 mg every other day for 6 months. At the end of that time there was definite improvement in the paresthesias but the ankle jerks were absent. Vibration and position sense remained intact. The glossitis had disappeared. Several months later the patient was completely free of neurologic signs and symptoms. He was then receiving daily 15 yeast tablets, 3 cod-liver oil tablets and 3 mg of thiamine chloride orally. He continued this treatment, and when seen 4 years later still had no complaints and showed no neurologic abnormalities.

Comment: In this case the neurologic symptoms began while the diabetes was out of control and became more pronounced following regulation of the diabetes. The subjective improvement preceded the disappearance of objective neurologic abnormalities. Under intensive vitamin therapy, definite subjective improvement occurred after 4 months and was followed by complete recovery in 1 year. It is worthy of note that the neuropathy continued to improve while under treatment with parenteral thiamine, despite a period of omission of oral yeast therapy because of diarrhea.

CASE 6 I C (B I H 64290A), a 59-year-old woman was found in November, 1940, to have diabetes. During the next 2 months, while the diabetes was being controlled by diet and insulin, she complained of anorexia, weight loss, crampy pain in the epigastrium and precordium and pains and paresthesias in the lower extremities. The right knee jerk was absent, and there was diminished vibration sense in both legs, more marked in the left than in the right.

Because of the persistence of abdominal pain, anorexia and continued weight loss, repeated gastrointestinal studies were carried out during the ensuing 4 months. These were negative except for a suspicion of small stones in the gall bladder. Blood-cell counts, the sedimentation rate, the blood chemical findings and the basal metabolism were normal. A blood Hinton reaction was negative. Examination of the spinal fluid on two occasions showed total protein contents of 167 and 182 mg per 100 cc but no other abnormalities. During these 4 months the diabetes was under constant control.

The patient received an intensive 2-week course of vitamin therapy consisting of 20 mg of thiamine chloride and 2 cc of vitamin B complex parenterally each day. For the next 6 weeks she was bedridden because of weakness of the legs and received no vitamins. The abdominal pain continued, but the diabetes remained under control and there was no change in weight. At the end of the 6-week period there was weakness of the lower extremities and an unsteady gait, and the patient had difficulty in rising from a chair. Both knee jerks and ankle jerks were absent. There was moderate tenderness of the calves and thighs. The paresthesias in the left foot had disappeared.

During the next 6 months 25 mg of thiamine chloride parenterally and 15 yeast tablets were given daily. The appetite improved and there was a gain in weight. The abdominal pain gradually subsided, and at the end of the 6 months the patient was free of subjective complaints. During the next 2 months she received only 12 mg of thiamine chloride twice weekly, the dosage of yeast tablets remaining unchanged. Three months later she had gained 22 pounds, felt well and had no difficulty in walking. Three years later she was still in good health. The knee jerks were present and equal, but vibration sense in both legs was still diminished.

Comment: In this case myelopathy developed soon after the control of an acute stage of diabetes that was accompanied by marked loss of weight. The symptoms of abdominal pain, loss of weight, anorexia and weakness suggested gastrointestinal malignancy, but the neurologic examination warranted the diagnosis of diabetic neuropathy after malignancy had been ruled out. Subjective neurologic complaints preceded the objective signs and disappeared first.

Clinical recovery followed 6 months of vitamin therapy.

CASE 7 H G (B I H 65326A), a 46-year-old man, was first seen in April, 1941, with acute manifestations of diabetes mellitus, which had been discovered 18 months before. He had had for 1 year paresthesias and weakness of both feet and more recently intermittent claudication, especially of the left leg. Pulsation of the left dorsalis pedis artery could not be distinctly felt. Calcification of the arteries of the legs could not be demonstrated by x-ray examination.

Four months later the intermittent claudication of the left leg had become severe. The patient also complained of weakness in the left foot. The diabetes had been incompletely controlled by diet and insulin. Examination showed sluggish jerks and ankle jerks and a diminution of vibratory sensation in both legs.

One month after daily injections of 25 mg of thiamine chloride and daily feeding of 15 yeast tablets had been begun, the patient was able to walk four times as far as previously. After 3 months of this therapy the intermittent claudication and all other neurologic symptoms cleared up completely, although the diabetes remained poorly controlled.

Comment: In this case the neuropathy developed during an acute stage of diabetes. It became worse after insulin was begun and progressed for 4 months until thiamine and yeast were administered. The symptoms then disappeared within 3 months, only to recur 2 years later after a long period of poor diabetic control and omission of vitamin therapy. Intermittent claudication was a possible manifestation of thiamine deficiency; it was not attributable to peripheral vascular sclerosis.

CASE 8 S C (B I H 43964A), a 74-year-old woman, was first seen in April, 1943, after many years of diabetes controlled by diet and insulin. Three weeks before entry she developed bronchopneumonia and was successfully treated with sulfadiazine. During convalescence, however, she developed nausea, vomiting, anorexia and incontinence of feces and urine. The tongue was smooth along the edges and red. There was a large, noninfected bed sore over the right iliac crest. The rectal sphincter was patulous and without tone.

An occasional finding in diabetic patients in the absence of definite neurologic signs is an unsteady gait or a tendency to fall. This is usually due to muscular weakness, which, although not severe at rest, may on walking progress to the point of bringing the patient to a halt or even causing him to fall. A related phenomenon is pain in the calf of the leg of the intermittent claudication type, which, although ordinarily ascribed to peripheral sclerosis, is not infrequently observed in patients with other signs of diabetic neuropathy. This manifestation of thiamine deficiency has been observed in beriberi and has been attributed to impaired carbohydrate metabolism and the resultant abnormal accumulation of metabolites in muscles.²³ Atony of the bladder with urinary retention, sometimes seen in the diabetic patient in the absence of neurologic signs,²⁴ may have the same pathogenesis.

Occasionally, diabetic neuropathy is also accompanied by isolated muscle atrophies that may be mistakenly attributed to the local effect of injected insulin. Such atrophies have, however, been observed in muscles remote from the site of injection⁶ and even in patients who are not taking insulin.

I consider diabetic neuropathy a manifestation of a diffuse disturbance that may involve the entire nervous system, thus producing a neuropathy of disseminated distribution. Manifestations of vitamin B complex deficiency are frequently associated with the neuropathy and improve simultaneously with the neurologic disorder on vitamin therapy. A few illustrative cases will serve to demonstrate these points.

CASE REPORTS

CASE 1 R M (B I H 43220), a 65-year-old woman, was first seen in September, 1938. Diabetes had been discovered 3 months previously and had been easily controlled, at first by diet and later by the addition of small doses of insulin. Despite control of glycosuria, there was generalized pruritus, furunculosis and carbuncles. The patient became progressively confused and resistive and developed paranoid trends.

Examination showed a red, beefy tongue and cheilosis. The gait was ataxic, and there was a positive Romberg sign. There was impairment of vibration and position sense in both legs. The left knee jerk was absent, and both ankle jerks were diminished. There was a Babinski sign on the left.

The patient was given a high-calorie diet, yeast tablets by mouth and daily injections of 10 mg of thiamine chloride. After 3 months of this regimen the skin lesions had completely cleared, but the knee jerks and ankle jerks had disappeared and the mental state remained unchanged. There developed in addition a short episode of weakness of the internal rectus and right facial palsy. After 4 months of vitamin therapy the mental state improved. Nevertheless, parenteral thiamine and yeast were continued, and 15 months later the patient was mentally completely normal. At that time the knee jerks and ankle jerks were still absent. The tongue, lips and skin were normal. Death from coronary thrombosis occurred 6 months later.

Comment. This patient developed mouth and skin lesions and evidence of a diffuse disseminated neuropathy of the brain and spinal cord after treatment of diabetes had been instituted. The tongue lesion and psychosis suggested a vitamin deficiency of pellagrous nature. Following prolonged vitamin B therapy there was complete mental recovery, with disappearance of the skin and mouth lesions, but some neurologic residual persisted.

CASE 2 L P (B I H 13642A), a 67-year-old man with mild diabetes of 4 years' duration, was admitted to the hospital in August, 1940, for hemorrhaphy. The urine was sugar-free, and the blood-sugar level was normal. Following operation he developed urinary retention due to prostatic enlargement. He was unable to eat and received several intravenous infusions of glucose but no vitamins. He became anemic and lost weight. One month later it was discovered that he had developed foot drop on the right and weakness of the left foot. The diabetes had been under control without insulin throughout the hospital stay.

Examination revealed weakness of the dorsiflexors of the feet, with complete foot drop on the right and diminution of sensation in the distribution of the peroneal nerve. There was marked diminution in the vibratory sensation in both lower legs, and the ankle jerks were hypoaesthetic.

The patient was given a high-vitamin diet with a concentrated vitamin B complex preparation by mouth and injections of 30 mg of thiamine chloride daily for 1 month. The right lower leg was put in a cast and later was fitted with a brace. Motor power gradually returned, and the brace was discarded after 6 months. Four years later there were no neurologic symptoms or signs. Muscle power in both feet was good. The knee jerks and ankle jerks were active and equal. There was no sensory defect. Vibratory sensation in both feet was normal.

Comment. In this patient with mild diabetes under constant control, neurologic symptoms developed as a result of a combination of insufficient food and vitamin intake, together with frequent glucose infusions and anemia. Recovery was subjectively and objectively complete after 6 months of intensive vitamin therapy.

CASE 3 E C (B I H 39066A), a 37-year-old man with a history of chronic alcoholism, was first seen in June, 1935, with symptoms of diabetes of 1 year's duration, during which time he had lost 74 pounds in weight. The diabetes was controlled in 2 weeks by diet and insulin. At the end of that time the patient complained of pains and paresthesias, first in the right arm and neck and later in the groins, scrotum and outer aspect of the right thigh. He also had paroxysmal attacks of girdlelike pain around the chest and severe burning sensations in the lower extremities and genitalia, especially at night. He complained of general weakness and repeatedly had to return to bed. He continued to lose weight on a high-calorie, high-carbohydrate diet, despite a marked improvement in the diabetes and a reduction in the insulin requirement from 60 to 6 units a day.

Early in the illness, neurologic examination revealed only absence of ankle jerks, but later there developed inequality of knee jerks and weakness and hyperesthesia of both lower extremities.

From the beginning, the patient had been given in addition to a proper diet and insulin large amounts of Harris's yeast powder by mouth. After 4 months of this therapy marked subjective improvement began. In 6 months he was free of neurologic complaints and had regained 10 pounds in weight.

Comment. In this alcoholic patient, the acute symptoms of diabetes had been present for over a year with marked loss of weight. The neurologic manifestations, however, developed 2 weeks after the treatment of diabetes was begun and for a while became progressively worse in spite of complete control and marked improvement of the diabetes. The subjective manifestations of neuropathy preceded by some months the objective signs, but they all finally cleared after 6 months of yeast therapy.

CASE 4 H V (B I H 29225), a 54-year-old woman with a history of diabetes treated by diet alone, was admitted to the hospital in November, 1935, in diabetic coma. She had recently lost 20 pounds in weight. Ten days after recovery from the coma, and after the diabetes had been satisfactorily controlled, she complained of excruciating paroxysmal pain in the lower back, especially on the right, and in both thighs, requiring the frequent administration of morphine. Examination revealed absence of tendon reflexes in the arms and legs, a sensory level at the 12th thoracic segment and loss of vibratory sensation below this level. One month later, when allowed to get out of bed, the patient showed unsteadiness of gait and ataxia of the legs and was unable to walk without support. She also displayed marked weakness and atrophy of the muscles of both legs, diminution of vibration sense on the right, loss of position sense in both feet, a positive Rom-

The prognosis for recovery from diabetic neuropathy is fair, and in some cases even good

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PNEUMOCOCCAL PERICARDITIS TREATED WITH INTRAPERICARDIAL PENICILLIN*

Report of a Case

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THE effectiveness of penicillin in the treatment of many varieties of pneumococcal infections is well established. Since it is believed that its effectiveness in a proved case of pneumococcal pericarditis is worth recording, the following case is presented

F. D., a 50-year-old shipyard office worker, was admitted to the Northern Permanente Foundation Hospital on April 8 1945, complaining of severe knifelike chest pains and dyspnea. Four weeks prior to admission he developed pleuritis on the left side, associated with some coughing, which was relieved by heat and strapping. Three weeks prior to admission he developed substernal pain, which was made worse by coughing. Severe dyspnea and orthopnea were present for 3 weeks, becoming progressively worse, but there was no ankle swelling. There was fever during the week prior to admission, the temperature rising as high as 104° F., but no severe shaking chill. Three weeks prior to admission a tooth was extracted. The past and family histories were noncontributory.

Physical examination revealed an extremely dyspneic and orthopneic man, who was moderately apprehensive. There was a granulating tooth socket in the right upper jaw, without drainage. The lungs showed dullness and diminished breath sounds over the left lower lobe posteriorly. Cardiac dullness extended to the anterior axillary line. The point of maximum impulse was not palpable. The heart sounds were faint and distant. Sinus tachycardia was present. In the 2nd interspace at the left sternal border was a loud to-and-fro pericardial friction sound, transmitted to the apex but faint there. The liver and spleen were not felt. There was no edema.



FIGURE 1

The temperature was 103° F., the pulse 150, the respirations 32, and the blood pressure 110/80. The white-cell count was 19,500, with 84 per cent neutrophils, 8 per cent of which were

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There was a large fecal impaction, and the mucosa of the rectum was prolapsed. The knee jerks were absent. The diabetes was under control.

The patient was given a daily dosage of 2 cc of vitamin B complex, 100 mg of nicotinamide and 120 mg of thiamine chloride parenterally. After 18 days the fecal and urinary incontinence disappeared and the decubitus ulcer completely healed. The patient continued to receive 2 cc of vitamin B complex parenterally each day. Two months after discharge the knee jerks were hyperactive, vibratory sensation was normal, and there was no incontinence. Fifteen months later no neurologic disturbances had recurred.

Comment. This is a case of an acute onset of diabetic neuropathy with manifestations of a vitamin B complex deficiency and rapid recovery following parenteral vitamin B therapy.

DISCUSSION

There appears to be no direct relation between the duration or severity of diabetes and the presence of neuropathy. The relation of neuropathy, however, to the onset, exacerbations and treatment of diabetes is of special interest and importance. In a few cases, the neurologic abnormalities develop before glycosuria is discovered. In others, they appear during the acute stage of diabetes (Cases 2, 3 and 6). In still others, they appear to be precipitated by other complications of the diabetes (Cases 5 and 8) or by the control of diabetes, whether by diet alone or by diet and insulin (Cases 1, 3, 4 and 6).

In most patients with diabetic neuropathy, there are observed many of the manifestations of experimentally induced thiamine deficiency in man, such as easy fatigability, forgetfulness, irritability, nausea, weight loss and personality changes (Cases 5 and 6). There may be evidence of additional deficiency of nicotinic acid, of riboflavin or of both (Cases 1, 5 and 8), for manifestations of deficiency of the vitamin B complex are frequent in diabetic patients.²⁴⁻²⁶ Moreover, the progression, disappearance and recurrence of the neuropathy parallel the course of other manifestations of deficiency of the vitamin B complex as altered or influenced by vitamin therapy (Cases 1 and 5). Since many patients with diabetic neuropathy frequently fail to improve on thiamine alone, they should be treated with the entire vitamin B complex in addition, parenterally if necessary.

Whatever may be the relation of diabetes to neuropathy or to vitamin deficiency, particularly to deficiency of thiamine, the importance of the latter to the physiologic activity of nerve tissue has been demonstrated by Nachmansohn and Steinbach.²⁷ These authors showed that thiamine is essential to the oxidation of pyruvic acid, a reaction that in turn provides the acetate required for the formation of acetylcholine. Since acetylcholine is necessary for the conduction and transmission of nerve impulses, a decrease in the rate of formation of this substance may lead to the motor disturbances observed in diabetic neuropathy. Other mechanisms,

such as functional or organic changes in the myelin sheaths,¹¹ must be postulated to explain the sensory changes that are also found.

Although the manifestations of vitamin B complex deficiency associated with uncomplicated poor nutrition are typical and respond dramatically to specific therapy,²⁸ the manifestations of the same deficiencies in diabetic patients are often atypical, frequently occur with apparently adequate diets and usually respond more slowly to the same treatment than in patients without such diabetes. These differences suggest a basic physiologic difference in the mechanism by which the deficiency manifestations are produced.

Govier and Greig²⁹⁻³¹ showed that in shocked or anoxic dogs cocarboxylase might dephosphorylate and become inactive. Similar inactivation of coenzyme I and of alloxazine adenine dinucleotide also occurred. The administration of large amounts of thiamine, riboflavin and nicotinamide resulted in the resynthesis of the respective coenzymes. Since these substances ultimately function as coenzymes in carbohydrate metabolism, it is possible that in diabetes a comparable metabolic disturbance underlies the manifestations of vitamin B complex deficiency and their improvement through large doses of vitamin B complex.

In nondiabetic patients, recovery from polyneuropathy induced by diets partially deficient in thiamine requires many months of thiamine therapy.³¹ It is therefore not surprising that recovery from diabetic neuropathy is often slow, particularly since the process when first recognized may have been of long duration. Hence, treatment of diabetic neuropathy may have to be continued for several years (Case 1) with massive doses of thiamine and of vitamin B complex parenterally before the process is arrested or alleviated. In an analogous situation, the combined system disease of pernicious anemia responds even more slowly to treatment than does diabetic neuropathy. At a very early stage, however, the diabetic neuropathy may still be of a functional or biochemical nature and may therefore respond quite rapidly to specific treatment.

SUMMARY AND CONCLUSIONS

Diabetic neuropathy is a disseminated neurologic disturbance that may involve any part of the nervous system.

The mere control of glycosuria, with or without insulin, does not prevent the development of diabetic neuropathy. The chronic and severer manifestations of diabetic neuropathy demand intensive and prolonged therapy.

The treatment of choice consists of large doses of thiamine chloride and vitamin B complex, parenterally if necessary, in addition to control of the diabetes.

MEDICAL PROGRESS

HEMOGLOBINEMIA AND THE HEMOGLOBINURIAS*

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BLACKWATER, or more scientifically, hemoglobinuria, attracts the attention of patient and physician as do few other symptoms. Indeed, few other symptoms indicate so serious a disturbance of body processes or carry so grave a prognosis. The diseases producing or associated with hemoglobinuria, with some exceptions, usually either have a high fatality rate or are extremely chronic and disabling.

It is the purpose of this paper to review the mechanisms by which hemoglobinuria is produced, to consider its pathologic effects and to summarize the important features of the clinical syndromes that lead to the excretion of hemoglobin in the urine.

PATHOLOGIC PHYSIOLOGY OF HEMOGLOBINEMIA AND HEMOGLOBINURIA

Normally in the human adult approximately 19 per cent of the circulating erythrocytes are destroyed each twenty-four hours, resulting in the liberation of between 7 and 8 gm of hemoglobin. Destruction of these erythrocytes takes place in the cells of the reticuloendothelial system, and the hemoglobin released as a result of their breakdown is metabolized by the reticuloendothelial cells into bilirubin, which is subsequently excreted in the bile by the polygonal cells of the liver. Theoretically, this process is an intracellular one and hemoglobin does not escape into the circulating blood plasma. Actually, however, 100 cc of normal human plasma contains 2 to 5 mg of heme-containing pigment derived, perhaps, from actual "intravascular" breakdown of erythrocytes.

In certain disease states, the rate of erythrocytic breakdown sometimes is increased by as much as fiftyfold, with liberation of 400 to 500 gm of hemoglobin within a period of twenty-four hours. In some conditions, for example, familial hemolytic jaundice, the erythrocyte destruction and hemoglobin breakdown continue as an intracellular process and the increased pigment catabolism is reflected only by an elevation of the plasma bilirubin concentration and an increased excretion of bilirubin. In other diseases, such as the acute hemolytic processes encountered in sulfonamide toxicity or incompatible blood transfusions, the destruction

of erythrocytes occurs intravascularly without the aid of the reticuloendothelial system. Hemoglobin is liberated directly into the blood plasma, with the result that its concentration in the plasma may increase to 400 or 500 mg per 100 cc, or higher. Hemoglobinemia may occur as a result of many different factors, but the mechanics of pigment metabolism are much the same, regardless of the primary cause of the hemolytic mechanism.

Hemoglobin liberated intravascularly first appears in the plasma as oxyhemoglobin, and if its concentration in the plasma is relatively low (50 to 100 mg per 100 cc), this is the only pigment that can be detected spectroscopically. Small amounts of oxyhemoglobin are rapidly removed from the blood plasma in four or five hours — primarily by the reticuloendothelial system. If, however, hemolysis is so extensive that large amounts (200 to 500 mg per 100 cc) of hemoglobin accumulate and remain in the plasma, an entirely different set of circumstances ensues. The hemoglobin molecule breaks down into hematin (the iron-porphyrin pigment complex) and globin (the protein fraction of hemoglobin). The hematin immediately combines with plasma albumin, and a new pigment, methemalbumin, is formed. There is good experimental evidence that oxyhemoglobinemia is innocuous, but it is quite possible that methemalbumin exerts a toxic effect on various organs and tissues.

Methemalbumin was first described by Fairley and Bromfield,^{1,2} who noted its presence in several cases of severe blackwater fever. It should not be confused with methemoglobin, which is usually intracellular in location and is rarely present in the plasma. In contrast, methemalbumin is encountered only in the plasma. Although methemalbumin resembles methemoglobin in the fact that the iron molecule in the prosthetic group of both compounds is in the oxidized or ferric state, its presence in the blood has an entirely different diagnostic and prognostic significance.^{3,4} Small amounts of methemoglobin occur normally in human blood,⁵ but methemalbumin never occurs normally and is encountered only in conditions of severe intravascular hemolysis with prolonged high concentrations of hemoglobin in the plasma. Methemoglobin is readily reconverted to oxyhemoglobin in the red blood cell,⁶ but methemalbumin cannot be reconverted either to methemoglobin or to oxyhemoglobin, and must be disposed of by the body in some other fashion, presumably by the reticuloendothelial system through conversion to bilirubin.^{3,4}

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stab cells. The red-cell count was 4,600,000 and the hemoglobin 13.2 gm.

An x-ray film taken on admission (Fig. 1) was interpreted as compatible with a pericardial effusion, left pleural effusion and vascular engorgement. An electrocardiogram showed no

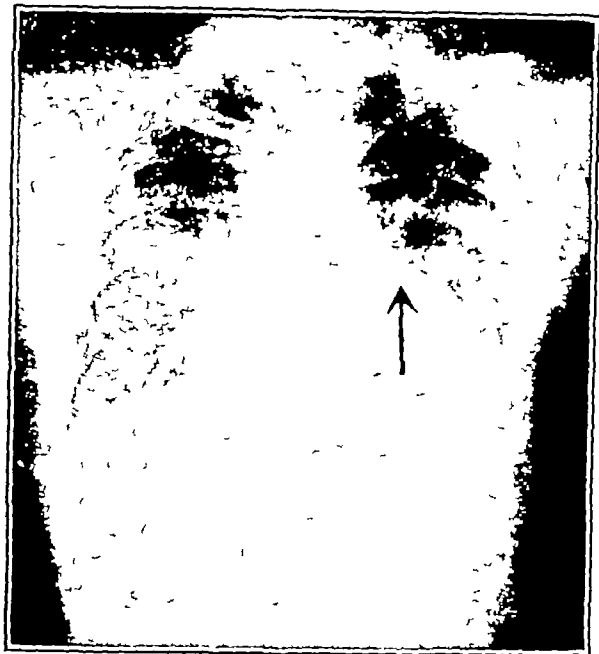


FIGURE 2

specific evidence of pericarditis, and the voltage was within normal limits, T₂ was diphasic. A blood culture was sterile. The venous pressure was equivalent to 160 mm. of saline solution.

The patient was given 10,000 units of penicillin every 3 hours intramuscularly and full doses of sulfadiazine with sodium bicarbonate, on the presumption that the infection might be a coccal one, and supportive therapy consisting essentially of oxygen and morphine, which made him more comfortable.

On the premise that a purulent pericarditis was a possibility, and since it is known that coccal infections of serous cavities, such as the pleural, subarachnoid and synovial types, respond to locally introduced penicillin, it was decided to do a pericardial paracentesis and instill penicillin. The tap was done on the day of admission in the 5th anterior interspace at the midclavicular line, with novocain infiltration. Since fluid was obtained with the infiltrating 22-gauge needle, the procedure was continued without removing the needle. One hundred cubic centimeters of a thin sanguineous fluid was removed. Twenty thousand units of penicillin were injected, even though the bacteriologic character of the fluid had not yet been evaluated, since it was thought that no harm could result and that a subsequent tap could be avoided should organisms be found. In addition, 10 cc. of air was instilled and another x-ray film was obtained. The fluid level then seen in the pericardium (Fig. 2) proved that the fluid was not being withdrawn from the pleural cavity. It contained 250,000 red cells and 2500 white cells per cubic millimeter, with 90 per cent polymorphonuclear leukocytes. No organisms were seen in a gram-stained smear, and an acid-fast stain was also negative.

In 36 hours a broth culture of the pericardial fluid yielded a gram-positive diplococcus, which examination by the Quelling technic showed to be a Type 8 pneumococcus. In view of this fact, a second pericardial paracentesis was performed on April 10 with a 22-gauge needle, and 150 cc. of fluid was removed, 15,000 units of penicillin being inserted. The fluid had a specific gravity of 1.020 and contained 94,000 red cells and 11,000 white cells per cubic millimeter, with 88

per cent polymorphonuclear leukocytes. No organisms were found in the smear, and a culture was sterile.

The penicillin dosage was increased to 20,000 units every 3 hours. The patient improved gradually, but remained febrile. On the 5th day, because of x-ray evidence of increasing effusion at the base of the left lung, a thoracentesis was performed and 500 cc. of a deep yellow fluid was removed with ease. The fluid clotted on standing, so that a cell count could not be obtained. A gram stain and culture were negative. No acid-fast organisms were found.

The venous pressure on the 6th day was equivalent to 96 mm. of saline solution. After running a low grade fever for several days, the patient became afebrile on the 10th day, remaining so thereafter. Chemotherapy was discontinued on the 12th day. The pericardial friction was not heard after the 8th day. The remainder of the course was uneventful, and the patient was discharged on April 30, the 20th hospital day. When seen again on June 14, 1945, he was asymptomatic and was working. The cardiac examination and follow-up x-ray examination (Fig. 3) were both negative.

Although it cannot be stated with certainty that the intrapericardial penicillin was responsible for the cure of this patient, it is fair to assume that it played an important contributory role. This assumption seems justified in view of the fact that it is well known that the treatment of pleural and synovial infections is much more successful when

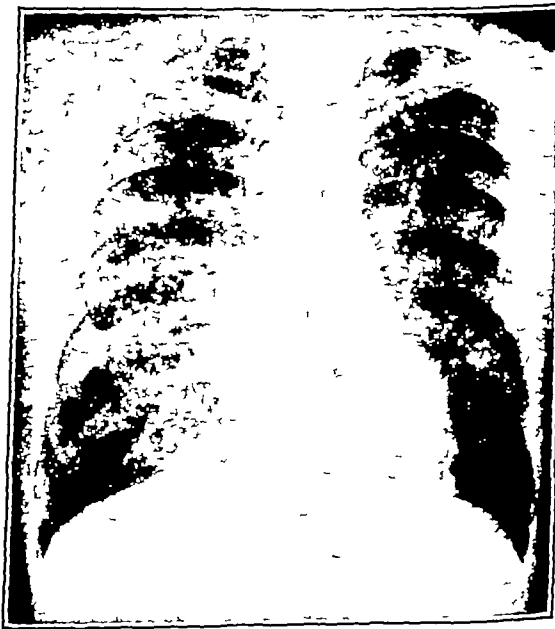


FIGURE 3

the local use of penicillin supplements parenteral penicillin.

SUMMARY

A case of Type 8 pneumococcus pericarditis successfully treated with penicillin intrapericardially, as well as with sulfadiazine and intramuscular penicillin, is presented.

Deposits of iron-containing pigment can readily be demonstrated in these cells after injections of hemoglobin, and the iron content of the kidney is markedly increased following multiple injections of hemoglobin.¹² Presumably this iron is eventually returned to the body for reuse in hemoglobin synthesis.

If the tubular cells become filled with iron-containing pigment, their capacity to absorb hemoglobin is interfered with, and as a consequence the renal threshold for hemoglobin may fall by as much as 60 per cent.^{13, 14} Such a decrease in threshold is seen following repeated injections of hemoglobin and in certain cases of chronic hemoglobinuria, for example, paroxysmal nocturnal hemoglobinuria. In the latter, the tubular cells become so filled with iron-containing pigment that they are cast off and appear in the urine, where they may be readily identified.

When excreted in alkaline urine, hemoglobin is found chiefly as oxyhemoglobin. In acid urine, and in urine that remains in the bladder or is allowed to stand *in vitro* for any length of time, considerable amounts of methemoglobin are found.

The mechanism of excretion of myoglobin probably is similar to that of hemoglobin, but because its molecular weight is only 17,500 in contrast to 68,000 for hemoglobin, there is a marked quantitative difference. The threshold for renal excretion of myoglobin is only 20 mg per 100 cc of plasma, and the rate of clearance is twenty-five times more rapid than that of hemoglobin. Consequently, myoglobin is removed from the blood stream so rapidly that it is difficult to demonstrate it in the blood plasma.¹⁵

PATHOLOGIC EFFECTS OF HEMOGLOBINEMIA AND HEMOGLOBINURIA

The sequence of hemoglobinuria, anuria, uremia and death following transfusion of incompatible blood¹⁶⁻¹⁸ and in blackwater fever¹⁹ as well as the demonstration of tubular occlusion by hemoglobin casts in the kidneys of such cases, led to the belief that passage of hemoglobin through the kidney produced serious and irreversible renal damage. Considerable experimental evidence supported this hypothesis.²⁰⁻²³ Yorke and Nauss,²⁰ Baker and Dodds²¹ and DeGowin et al.^{22, 23} injected solutions of hemolyzed erythrocytes into experimental animals (rabbits and dogs) and reported that these animals frequently became anuric, developed uremia and died of renal failure if the urine was acid during the period of hemoglobinuria. If the urine was alkaline in reaction, there were no ill effects from the excretion of hemoglobin.

Histologic examinations showed that many renal tubules were occluded with hemoglobin casts in those animals that had had an acid urine, but that the kidneys were relatively normal in animals whose urine had been alkaline. Observations such as these

indicated that hemoglobin damaged the kidney only if the urine was acid during the period of hemoglobinuria, and explained this damage as due to the precipitation of acid hematin in the renal tubules, with subsequent mechanical blockage of urine flow. This theory led to the widespread therapeutic use of alkalis in an attempt to alkalinize the urine in patients with hemoglobinuria from transfusion reactions,¹⁷ blackwater fever²⁴ or other causes.

In marked contrast to these observations are numerous experiments that have conclusively demonstrated that solutions of pure hemoglobin can be injected intravenously into normal human subjects and into experimental animals without producing any significant impairment of renal function, regardless of the reaction of the urine.^{2, 25-31} Many of these studies have been performed within the last five years and have been made with carefully prepared solutions of hemoglobin, in some instances with pure crystalline hemoglobin. Careful observations of the clinical condition of the subjects revealed that as much as 20 gm of hemoglobin might be administered without any ill effect. In some cases abdominal cramps and fever occurred, but these well might have been caused by the presence of histamine-like substances or potassium in the hemoglobin preparations employed.³⁰ The most thorough evaluation of the effect of hemoglobinemia, myoglobinemia and methemoglobinemia on kidney function has been made by Bing.³¹ Solutions of pure crystalline hemoglobin, myoglobin and methemoglobin were infused into normal dogs and into dogs made acidotic by the oral administration of ammonium chloride. Studies were made of the glomerular filtration rate and of the effective renal plasma flow in all animals, and in some experiments tubular reabsorptive capacity also was measured. Following infusion of large amounts of hemoglobin and myoglobin there was no significant variation in renal function, and histologic examination revealed no lesions of any type, even in those animals in which the reaction of the blood had been reduced to pH 6.90. Injections of methemoglobin produced no functional or anatomic changes in normal dogs, but in all the animals that were acidotic, methemoglobinemia and methemoglobinuria produced a marked decrease in clearance values (10 per cent of the control values), the absorptive capacity of the renal tubules for glucose decreased, nitrogen was retained, and the dogs rapidly became moribund. Histologic examination of the kidneys of the acidotic animals revealed marked tubular necrosis, but pigmented casts were found in the tubular lumens only in those acidotic animals that received repeated infusions of methemoglobin after renal failure had been initiated. These observations indicated that the precipitation of hemoglobin products in the tubules, far from being an important cause of anuria and renal failure, was actually the result of a decreased volume of urine

Sulfhemoglobin, a third abnormal blood pigment, is encountered even more rarely than methemoglobin or methemalbumin. Like methemoglobin, it almost always is an intraerythrocytic pigment, but it occasionally occurs in the plasma in certain hemolytic diseases with associated intoxications.³

Myoglobin and its ferri-derivative, metmyoglobin, appear in the urine following crushing injuries, but owing to the rapid rate at which these substances are removed from the blood stream, it is unusual to detect them in the blood plasma.⁷

Detection of these abnormal heme pigments is a simple matter, and frequently may be of considerable value in diagnosis and prognosis. Methemalbumin, methemoglobin, sulfhemoglobin and metmyoglobin are characterized by a distinct absorption band in the red portion of the spectrum, and the presence of such a band may be readily demonstrated with an inexpensive hand spectroscope, frequently by the simple expedient of sighting the instrument through the well illuminated auricle or lobe of the ear. The absorption maximums of the various heme pigments are listed in Table 1. Although the alpha bands of the various met-compounds have characteristic wave lengths, they differ in situation by only a few Angström units,

TABLE 1 *Absorption Maximums of Heme Pigments*

PIGMENT	WAVELENGTH OF ABSORPTION MAXIMUMS		
	ALPHA mμ microns	BETA mμ microns	GAMMA mμ microns
Metmyoglobin	636	580	—
Methemoglobin	630	576	541
Methemalbumin	623-624	540-541	500-501
Sulfhemoglobin	618-620	540	—
Myoglobin	581-582	545-546	—
Oxyhemoglobin	576	541	—

and with the spectroscopic instruments commonly available, it is difficult to differentiate one from another. Consequently, a few simple chemical tests are necessary to identify definitely the abnormal pigment once its presence in the blood, plasma or urine has been established. These tests depend on the dispersion or persistence of the alpha bands of the compound when a reducing or oxidizing agent is added to the solution. Such tests are outlined in Table 2.

When hemolysis is extensive or occurs rapidly, the concentration of hemoglobin in the plasma rises to high levels and hemoglobin appears in the urine. Since the hemoglobin molecule is approximately the same size as the plasma albumin molecule, and since hemoglobin is excreted freely by the normal kidney and albumin is not, it has been difficult to reconcile this phenomenon with the modern concept of glomerular filtration, that is, with the concept that the fundamental process in urine secretion is the formation by the glomerulus of a protein-free filtrate containing diffusible constituents of plasma in the same concentration as they exist in the plasma water.

The best explanation of the mechanism by which hemoglobin is excreted by the kidney was advanced by Havill, Lichty, Taylor and Whipple,⁹ subsequently elaborated by Monke and Yuile¹⁰ and sum-

TABLE 2 *Differentiation of Abnormal Blood Pigments in Serum, Blood or Urine**

REAGENT	PIGMENT AND POSITION OF ALPHA ABSORPTION MAXIMUM		
	METHEMOGLOBIN (630 mμmicrons)	METHEMALBUMIN (623-624 mμmicrons)	SULFHEMOGLOBIN (618-620 mμmicrons)
Sodium cyanide, 5%	Dispersed	Unaltered	Dispersed
Hydrogen peroxide 3%	Dispersed	Unaltered	Dispersed
Stokes' reagent (2 drops added to 1 cc)	Dispersed	Unaltered	Unaltered
Ammonium sulfide, 10% (1 drop added to 1 cc.)	Dispersed	Unaltered	Unaltered
Ammonium sulfide, concentrated (0.1 cc added to 1 cc)	Dispersed	Dispersed	Unaltered

*Modified from Fairley⁸ and Fox.⁸

marized in an excellent review by Yuile.¹¹ Carrying out their investigations in dogs, these investigators found that there was a definite renal threshold for the excretion of hemoglobin. No hemoglobin could be detected in the urine when the plasma hemoglobin concentration was below 100 mg per 100 cc, but when it exceeded 100 mg per 100 cc, hemoglobin appeared in the urine. At concentrations in excess of 250 mg per 100 cc, the rate of hemoglobin excretion varied directly with the concentration of hemoglobin in the plasma. Furthermore, by performing hemoglobin and creatinine clearance studies simultaneously, Monke and Yuile¹⁰ showed that when the plasma hemoglobin concentration was in excess of 250 mg per 100 cc the rate at which hemoglobin was excreted was always 3 per cent of the creatinine clearance.

These observations could best be explained by assuming that 3 per cent of the pores in the glomerular membrane were large enough to allow the passage of large hemoglobin molecules into the glomerular filtrate. As the filtrate passed down the renal tubules, the epithelial cells of the proximal convoluted tubules removed the hemoglobin molecules by a process that has been called "arthrocytosis." So long as the amount of hemoglobin passing through the glomerular membrane did not exceed 2 or 3 mg per minute, the epithelial cells recovered all the hemoglobin and hemoglobinuria did not occur. The capacity of these cells to take up hemoglobin was limited, however, and if larger amounts of hemoglobin leaked through the glomerulus, they were unable to assimilate it and hemoglobin appeared in the urine. The recovery capacity of the tubules was completely exceeded when the plasma concentration of hemoglobin exceeded 250 mg per 100 cc, and any further increase in the concentration in the plasma was reflected by a proportional increase of hemoglobin in the urine.

The tubular epithelial cells thus play an active role in the conservation of hemoglobin and iron.

The demonstration of this hemolysis with its characteristic properties of fixation by cold and curvation by warmth in the presence of complement known as the "Donath-Landsteiner reaction," and with the Ehrlich and Rosenbach tests it should be performed in all cases suspected of hemoglobinuria.

Since the reports of Donath and Landsteiner, there have been many investigations of the serologic mechanism of the disease. These have been summarized by Mackenzie⁴¹ in an excellent and extensive review on cold hemoglobinuria. The cold hemolysin, although usually occurring in persons with positive Wassermann reactions, is distinct from the Wassermann reacting substances; it is possible to remove the hemolysin completely from a given serum by absorption in the cold without changing the titer of the Wassermann reacting substance. Although there is no distinct parallelism between the titers of the autohemolysin and the Wassermann reacting substance, both substances decrease in concentration in patients receiving antisyphilitic treatment. When adequate therapy of this type is administered, the clinical manifestations of the disease cease, the Wassermann reaction becomes negative, and the autohemolysin disappears from the serum in the order named. In patients who receive no antisyphilitic therapy, however, the titer of the lysin remains remarkably constant for many years. The hemolysin is extremely thermolabile and may be destroyed by the techniques commonly employed for inactivation of complement.

Why an autohemolysin should develop in some patients during the course of a syphilitic infection is quite obscure. Mackenzie⁴¹ has speculated that the lysin may be formed as an antibody response to antigens released from infected visceral organs. This speculation was provoked by the experiments of Namba,^{42, 43} who was able to produce autohemolysins in syphilitic and nonsyphilitic rabbits by injecting them with emulsions of calf kidney and other organs not containing the Forssman antigen. He was able to produce hemoglobinemia in these sensitized animals by placing a rubber band around an ear and immersing it in ice water. These experiments are extremely interesting, especially in view of the fact that injections of such organ emulsions are capable of producing positive Wassermann reactions in nonsyphilitic rabbits.

Fluctuations in the titer of complement have been demonstrated in the blood of patients with cold hemoglobinuria.^{44, 45, 50} After frequent attacks the complement may decrease in concentration or completely disappear, and in some cases the serum may become anticomplementary. In spite of the complete absence of complement from the patient's serum, however, severe attacks of hemoglobinuria may occur following exposure to cold.⁵⁰ In view of these facts, the Donath-Landsteiner reaction should be carried out with washed erythrocytes and with the addition of fresh complement.

The clinical features of paroxysmal cold hemoglobinemia vary widely in severity but usually follow the same general pattern. Following exposure to cold, a latent period varying from a few minutes to several hours may elapse before the prodromal symptoms of malaise, muscle aches and pains, abdominal cramps and headache appear. These symptoms are soon followed by a severe shivering chill and a rise in temperature to 102 or 103°F. The first urine voided after the chill is red or black, and subsequent specimens may be similarly colored for a few hours or several days, depending on the severity of the attack and the extensiveness of the hemolytic process. Abdominal cramps may persist for several hours but are usually of much shorter duration. They are probably produced by vascular spasm and may be relieved by intravenous injections of calcium chloride solution. The fever subsides in the course of an hour or two, and the patient then may feel slightly weak or may be prostrated, depending on the severity of the hemolysis and the degree of anemia produced. Jaundice appears within a few hours after severe attacks and may be noticeable for a day or two.

Vasomotor disturbances occur frequently during both the prodromal period and the actual hemolytic crisis. They may vary in severity from hives and mild urticaria⁵¹ to extreme vasospasm of the type commonly seen in Raynaud's disease, with painful, cyanotic fingers, toes and ears.^{45, 52} Why these symptoms of sympathetic-nervous-system abnormality should occur is quite unknown. They are not noted in other clinical types of hemoglobinemia and hemoglobinuria, and it seems probable that they are causally related to the underlying syphilitic infection.

The blood picture varies with the severity of the hemolytic process, which usually is marked enough to produce a moderate degree of anemia. Occasionally attacks may be so severe that the number of red blood cells may be reduced to 50 per cent of their pre-attack level.^{46, 53} As in other types of hemolytic anemia, the bone marrow responds to the anemia with reticulocytosis and rapid blood regeneration.

Marked leukopenia develops during the course of the paroxysm, and the total white-cell count may drop to 1000 or even less^{54, 55} because of the virtual disappearance of granulocytes from the peripheral blood. Similar granulocytopenia is commonly encountered in other types of hemoglobinemia and may be the result of the intravascular liberation of the breakdown products of erythrocytes.⁴¹ Between attacks, the blood picture is normal or there is a moderate lymphocytosis.^{41, 54} Thrombocytopenia of marked degree may also develop during the paroxysm.⁵³

The amount of cold exposure necessary to produce the paroxysms varies markedly from patient to patient. Exposure to a temperature of 40°F. was

and renal failure De Navasquez²⁸ made somewhat similar observations on human subjects and on rabbits and concluded that the excretion of hemoglobin, even in acid urine, did not impair renal function and that renal damage occurring in transfusion reactions was brought about not by tubular blockage but by greatly decreased blood flow through the kidney and by tubular anoxemia

Of considerable interest in this connection are the observations of Mason and Mann³² and Hesse and Filatov,³³ who showed that injections of hemoglobin solutions produced marked spasm of renal blood vessels, disappearance of about half the working glomeruli and a marked and rapid decrease in the size of the kidney

Thus, the best available evidence indicates that in normal persons, hemoglobinemia and the excretion of moderate amounts of hemoglobin are without ill effects, regardless of the reaction of the urine The fact remains, however, that extreme intravascular hemolysis frequently is associated with fatal renal damage This damage is probably produced by shock-like levels of blood pressure and by severe and prolonged reduction of blood flow through the kidney Decrease in renal blood flow is accentuated by hemoglobinemia, and in cases of marked reduction in the alkali reserve, the formation of methemoglobin in the acid glomerular filtrate may aggravate already existing tubular damage Similar conclusions have been reached by Foy, Altmann, Barnes and Kondi,³⁴ in an excellent and extensive review of all published observations on hemoglobinuria

In addition to the renal lesions observed in severe intravascular hemolysis, extensive central hemorrhagic necrosis of the liver has been reported,^{16, 35} a lesion that might also be produced by low blood pressure, decreased blood flow and anoxemia

PAROXYSMAL COLD HEMOGLOBINURIA

Clear differentiation of hematuria and hemoglobinuria was made in 1854 by Dressler,³⁶ who described a case of paroxysmal hemoglobinuria in a patient with congenital syphilis but did not recognize the etiologic importance either of syphilis or of chilling In 1866, Gull³⁶ observed that exposure to cold precipitated attacks of hemoglobinuria, but he assumed that the shaking chill was instrumental in producing the hemoglobinuria Rosenbach³⁷ reported that an attack of hemoglobinuria could be precipitated by immersing the patient's feet in cold water for ten minutes, thus clearly proving the causal relation of chilling to the syndrome This procedure, now known as the "Rosenbach test," is of considerable value as a diagnostic procedure in differentiating cold hemoglobinuria from various other types of hemoglobinuria, but it is occasionally dangerous because of the severity of the paroxysms produced Ehrlich³⁸ found that the phenomenon of hemoglobinemia could be produced locally in susceptible persons by

placing a ligature around a finger and then immersing it in ice water, free hemoglobin being demonstrated in the serum of blood removed from the finger This, the "Ehrlich test," is less hazardous to the well being of the subject than the Rosenbach test and should be performed before the latter in the investigation of patients with hemoglobinuria

Götze³⁹ first recognized the significance of syphilis as the cause of cold hemoglobinuria, and subsequent investigations have indicated that the disease is usually, perhaps always, a manifestation of syphilitic infection Donath and Landsteiner⁴ reviewed the literature from 1905 to 1925 and found that of 99 cases reported, 95 had either clinical or serologic evidence of syphilis All of Mackenzie's 5 cases showed positive Wassermann reactions, and almost all the cases subsequently reported had positive serologic evidence of syphilis The incidence of congenital syphilis is especially high in cold hemoglobinuria⁴²

A small percentage of patients with late cases of syphilis show the presence of the cold hemolysis in their plasma, but only a few actually have symptoms of hemoglobinuria Donath and Landsteiner studied 93 patients with general paresis and demonstrated the cold hemolysis in the serums of 7, only 1 patient, however, had symptoms of paroxysmal hemoglobinuria Japanese investigators^{44, 45} have reported finding cold hemolysins in 20 to 25 per cent of patients with tertiary syphilis, an incidence much higher than that found by American observers In a study of 360 patients under routine antisyphilitic therapy in an outpatient clinic, Dill⁴⁶ found only one positive Donath-Landsteiner reaction, which suggests that the probability of development of cold hemolysins may be markedly reduced by proper antisyphilitic therapy

The fundamental abnormality existing in cold hemoglobinuria was not understood until the investigations of Donath and Landsteiner⁴⁷ They found that when a mixture of plasma and red blood cells from a patient suffering from paroxysmal cold hemoglobinuria was chilled in ice water and subsequently warmed to 37°C, marked hemolysis occurred The abnormality causing the hemolysis existed in the plasma rather than in the erythrocytes, since the patient's plasma was capable of hemolyzing normal red blood cells of the same blood group, but the patient's erythrocytes, mixed with normal plasma, showed no hemolysis after chilling and warming Inactivation of the plasma complement by heat prevented the hemolysis from occurring, but the addition of fresh guinea-pig complement restored its hemolytic activity Two phases of the reaction were demonstrated: absorption of the lysis on the erythrocytes at low temperatures, a fixation that occurred even in the absence of complement, and lysis of the sensitized erythrocytes when they were warmed, which occurred only if active complement was present

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31491

PRESENTATION OF CASE

First admission A sixty-three-year-old Italian was admitted to the hospital complaining of frequency, dysuria and diminution of the urinary stream of several months' duration. He had also complained of backache for an indefinite length of time.

For several years before admission the patient had complained of epigastric pain radiating beneath the sternum and to the back. The pain was relieved by food. Melena was present on one occasion at the onset of these symptoms. He was followed in the Out Patient Department, where a gastrointestinal series revealed a questionably active old duodenal ulcer. Two months before admission, hematemesis and melena again occurred. He was treated with aluminum hydroxide and a bland diet, and his symptoms were much improved at admission.

On physical examination the patient was obese and pale. He had had chorioretinitis for more than three years and was almost completely blind. The heart and lungs were normal, except for moist rales at the right base. Rectal examination revealed a small, soft, left prostatic lobe. The right lobe was firm, and there was no clear-cut sulcus between the right lobe and the pelvic wall, the apex of the prostate was not clearly defined. The reflexes were normal.

The temperature was 99°F, the pulse 80, and the respirations 20. The blood pressure was 160 systolic, 90 diastolic.

The red-cell count of the blood was 4,500,000, with 80 per cent hemoglobin. The white-cell count was 9000, with 60 per cent neutrophils. A blood Hinton test was negative. The urine was normal. The nonprotein nitrogen was 28 mg per 100 cc. An x-ray film of the chest was negative. The heart shadow was a little prominent in the region of the left ventricle. An intravenous pyelogram revealed small kidneys and normal function.

A transurethral resection was done, and microscopic examination of the fragments showed benign hyperplasia, there was no evidence of malignancy. The patient recovered uneventfully and was discharged improved.

*On leave of absence.

Second admission (two years later) The patient was followed in the Out Patient Department. The right lobe of the prostate remained firm for about a year but did not increase in size. He complained of angingal pain and exertional dyspnea. The cardiac rhythm was regular. An electrocardiogram showed slight left-axis deviation. A QRS complex was notched, and R₄ and T₄ were low. For ten months prior to readmission the induration of the right lobe of the prostate seemed to spread into the left lobe. He was readmitted to the hospital for further study.

Except for the prostatic induration, physical examination was negative. An x-ray film of the chest showed no evidence of metastases. The serum calcium was 10.8 mg per 100 cc, the phosphorus 2.5. The acid phosphatase was 3.3 units per 100 cc, and the alkaline phosphatase 3 units. Believing that the prostate was carcinomatous a bilateral orchidectomy was performed, following which the patient was discharged in good condition, with instructions to take 1 mg of stilbestrol twice daily.

Final admission (two and a half years later) The patient was again followed in the Out Patient Department, where one month after discharge the right lobe of the prostate was found to be markedly reduced in size but still extremely firm. The left lobe was soft. Stilbestrol was discontinued. Ten months later he complained of vague, transitory pain in the neck and back. Stilbestrol was again prescribed, the symptoms were relieved, and his general condition improved. Six months before readmission, however, he complained of pain in the right hip posteriorly. X-ray studies of the lumbar spine and pelvis showed no evidence of metastases. Two months before readmission, while turning on his left side in bed, he suddenly experienced sharp pain over the left chest, radiating to the left arm and later to the left leg. The pain persisted, with exacerbations, and was not relieved by the ingestion of food. There was no change in the character or color of the stools. For a month before readmission he vomited after almost every meal. Severe dyspnea was also present. He had lost no weight. He was again referred to the hospital.

Physical examination showed an obese, pale, and dyspneic man with grunting respirations. The chest was emphysematous, with numerous fine rales. The heart was negative. The abdomen was prominent, with no evidence of fluid. The liver was palpable three fingerbreadths below the costal margin, it was tender. There was no edema. The prostate was irregular but not hard.

The urine was normal. The red-cell count was 2,500,000, with 6.5 gm of hemoglobin. The white-cell count was 4900, with 44 per cent neutrophils. Three stool examinations were guaiac positive. The nonprotein nitrogen was 52 mg per 100 cc, falling later to 30 mg. The acid phosphatase was

required to produce attacks in Macalister's⁵⁵ patients, but Strominger and Gottfried⁵⁶ reported that their patients developed symptoms if exposed to a draft from an unheated room. One of Mackenzie's⁴¹ cases experienced spontaneous attacks while in bed in a hospital ward in the middle of the summer. Roch and Liengme⁵⁷ were able to produce paroxysms by giving their patients cold drinks.

As might be expected from the high renal threshold for hemoglobin, mild attacks of hemolysis may occur with accompanying hemoglobinemia but without hemoglobinuria.⁴⁴ Kaznelson⁵⁸ described a case with typical constitutional symptoms followed by jaundice but not by hemoglobinuria. Occasionally, hemoglobinuria may occur without constitutional symptoms.⁵⁹

(To be continued)

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Let us see some of the x-ray films, Dr. Hale. I am especially interested in the chest. Also, I wonder if there is any film that shows the upper dorsal or cervical vertebrae.

DR. CLAYTON H. HALE: This chest film, taken four years before the final admission, is reported as essentially negative, and I agree with that interpretation. This film was taken two years later and is also essentially negative except that there is a slight suggestion of enlargement of the left hilus. This third film was made this year and shows a large round shadow overlying the left hilus. This next film was taken about a month later, and because a portable machine was used it is difficult for me to be sure of any great change in the pulmonary vessels since the earlier examination. You will notice, however, that the left half of the diaphragm is high and that the hilar mass is more noticeable than it is on the previous film. It is completely covered by the heart shadow, but I am quite sure that it is an enlarged node in the left hilus.

DR. RICHARDSON: I thought you were going to say something about the linear shadows.

DR. HALE: I think the difference is explained by the fact that it was taken with a portable machine.

DR. RICHARDSON: Can you see any bone lesions?

DR. HALE: I do not see any abnormality in the ribs, no metastases are demonstrable.

DR. RICHARDSON: There is no osteoblastic activity?

DR. HALE: No. There is a deformed duodenal cap, with a crater in the central portion on the posterior wall. None of the films show the descending loop particularly well. I shall have to say that there is nothing definitely abnormal in the region of the ampulla, it is not too well demonstrated, however. The folds of the stomach look large in these films, but except for the possibility of retained secretions in the stomach at the time of examination, I should have to call the stomach normal. I cannot make out any areas of ulceration, nor can I see any evidence of rigidity of the wall.

DR. RICHARDSON: Do you see any linear markings in the lungs that look like healed infarcts?

DR. HALE: No.

DR. RICHARDSON: We have to explain why this man died. I do not believe that he had carcinoma of the prostate or that his prostate had anything to do with the terminal illness. We know that he was an Italian, and we have definite evidence that he had portal cirrhosis of the liver. We also have definite evidence that he had duodenal ulcer, and the combination of peptic ulcer and portal cirrhosis is not too unusual. Also portal cirrhosis in Italians, as I have pointed out many times, is frequently seen. The question is, Did this man have anything else besides that, or did he die as a result of surgical procedures that perhaps were not indicated? Morphine given preoperatively and postoperatively in a patient with cirrhosis of the liver is dangerous.

This man might also have had too many transfusions. My guess is that that is why he died, but I have not at hand the postoperative orders and I do not know whether he received morphine. If he did not, I am all wrong. You all know that in a patient with a sick liver any drug is likely to be dangerous, especially morphine. We have had several extremely disturbing results following the administration of morphine to patients with sick livers.

He may have had some other disease. He apparently did not have an infection. I see no evidence of miliary tuberculosis or anything of that sort, so that I should rather not mention infection. That brings us to tumor. If he had tumor, what sort of tumor was it? We have no evidence to help settle this question. He had an anemia, — a red-cell count of 2,500,000, — only slightly hypochromic by measurement. Of course, if I had a blood smear and a microscope I should not be in this difficulty! One can usually tell from a smear whether one is dealing with infection, tumor or blood loss. This man had apparent liver failure, however, he had also been known to bleed and had been vomiting. All these things can contribute to anemia of this degree. One cannot say that the anemia was not due to tumor involving a large part of the bone marrow, which can occur with negative x-ray films. One always has to think of lymphoma. There is nothing more to suggest it. I thought of lymphoma because of the x-ray report in the protocol, but the interpretation of the films that Dr. Hale has just shown makes it seem unlikely. I suppose a lymph node in this region could be due to a lymphoma as well as to anything else, but it does not suggest it to me. Does it to you, Dr. Hale?

DR. HALE: No.

DR. RICHARDSON: One might think of bronchio-genic carcinoma, with an enlarged lymph node, or of some other type of metastatic node.

We all know that hepatoma occurs in the presence of cirrhosis of the liver and only then. I say that, but I believe that we had one case without cirrhosis of the liver. Do you remember that, Dr. Sniffen?

DR. SNIFFEN: Yes, we have had one.

DR. RICHARDSON: In general, hepatoma occurs in the presence of cirrhosis of the liver. One has to consider hepatoma in this case. I see no way to rule it out or in. The whole thing comes down to the question, Did this man have a malignant tumor? How do we account for the pain, which I emphasized in the first place? I was going to say, and very likely I am going to stick to it, that it was not due to fracture, which it sounds like, when he turned over in bed and had a sharp pain, but rather to a sudden embolus and that he later on had pain in the calf of his leg from thrombophlebitis. I thought that I should see plenty of evidence of disease in the x-ray film of the chest, with old pulmonary infarcts, but I do not see anything there.

36 units. The gastric juice contained 15 units of free acid in a fasting specimen and 90 units after histamine stimulation.

X-ray examination of the chest showed diffuse nodular and linear density throughout both lung fields, slightly more marked on the left than on the right, extending toward the periphery. There were shadows suggestive of enlarged nodes at each hilus. The heart was normal. The diaphragm was low but showed fairly good respiratory motion. A gastrointestinal series revealed a wide esophagus, without definite varices. The stomach showed thickening of the mucosal folds and considerable narrowing of the antrum and prepyloric areas. A definite crater could not be demonstrated, although one plate showed a shadow suggestive of a crater at the angle. No peristalsis was seen along the greater-curvature margin of the area of narrowing. The duodenal cap was deformed, and in the narrowest portion there was a crater approximately 4 mm in diameter. The remainder of the duodenal loop was not remarkable. A barium enema revealed filling of the entire colon. The terminal ileum could not be filled, despite positioning and pressure. There was an area of narrowing in the sigmoid, not completely visualized because of gas in this area. Gastroscopy was negative.

The day after admission the patient vomited about 400 cc of cloudy, yellow, guaiac-positive fluid. He also complained of abdominal discomfort and gas. On the ninth day a peritoneoscopy revealed a hob-nailed liver, and biopsy showed mild portal cirrhosis. Three weeks after admission he complained of pain in the left side of his body, including the chest, abdomen and leg. The abdomen was markedly distended, and a fluid wave was present. Peristalsis was normal. There was tenderness to pressure over the transverse colon. There was no tenderness of the calf muscles. A cecostomy was performed.

Although the cecostomy drained well, abdominal distention persisted and the patient became apprehensive and disoriented. Dry, fine, crackling, inspiratory rales were heard at the left base, with dullness in the same area. An x-ray film of the chest was unchanged. Upper abdominal pain was present. A flat plate of the abdomen showed marked distention of the entire colon down to the lower sigmoid, with no air in the rectum. There was no evidence of small-bowel distention.

On the thirty-third hospital day an exploratory laparotomy was performed. The liver was cirrhotic, and there was a small amount of ascitic fluid. No neoplasm could be found in the bowel. There were extensive inflammatory adhesions around the sigmoid, but no evidence of obstruction. No diverticulitis was observed. After the operation the patient had labored respirations and expired on the second postoperative day.

DIFFERENTIAL DIAGNOSIS

DR WYMAN RICHARDSON. Epigastric pain radiating to the sternum and to the back is not inconsistent with the pain of duodenal ulcer, usually one on the posterior wall I should say.

I shall point out that an x-ray examination of the chest was negative, not only four years before admission but also two years later. The patient complained of anginal pain and exertional dyspnea. It is usually true that people with anginal pain do not complain of exertional dyspnea. Exertional pain would be anginal. I do not know whether or not we should pay much attention to the dyspnea. You will note that the serum calcium and phosphorus were normal, also the phosphatase. There was no evidence of osteoblastic activity, nor was there evidence of metastases from a carcinomatous prostate.

We then come to the time when the patient turned over on the left side and had the sharp pain. To me, that usually means a fracture and usually a pathologic fracture. The problem here is, Why does he have a fracture that gave him pain in the chest and in the arm and later in the leg? I cannot think of any one fracture that would do it. All these seem to have happened at about the same time. I should imagine that a fracture would have to be in the cervical region to produce pain in the arm. It should be a high upper dorsal vertebra or rib to produce pain in the chest, but by no means can I explain pain in the leg. One could explain pain in the chest radiating down the arm, followed later by pain in the leg, by a pulmonary embolus and later a thrombophlebitis in the leg. We shall have to consider that more seriously later. The degree of pain is not entirely clear, but it persisted with exacerbations and was not relieved by the ingestion of food. I do not imagine that the pain in the leg was due to ulcer, and probably not the pain in the chest, assuming that he had an ulcer.

The next thing to comment about is the large liver, which was three fingerbreadths below the costal margin. It may or may not have been a large liver, depending on the upper border of dullness. I am not going to be fussy and ask for that. One would not expect the patient to have a large liver from the peritoneoscopic findings.

Is there any record of the temperature at the final admission?

DR RONALD C SNIFFEN. Here is the chart.

DR RICHARDSON. It is a relatively flat temperature curve, with occasional spikes above 100°F by rectum, on one occasion reaching 101°. It does not suggest sepsis.

There was a lot of free hydrochloric acid after histamine. The stomach contained a large amount of fluid, 400 cc, and the fluid was yellow, which suggests that it contained bile and therefore indicates that there was not complete pyloric obstruction.

ecostomy, but I see no reason for the laparotomy except plain curiosity I do not believe that it was justified

DR. VOLWILER Certainly not without further x-ray evidence

CLINICAL DIAGNOSES

Carcinoma of sigmoid
Portal cirrhosis of liver
Duodenal ulcer

DR. RICHARDSON'S DIAGNOSES

Portal cirrhosis of liver
Peptic ulcer of duodenum and possibly stomach
Coronary sclerosis, mild
Thrombophlebitis, with pulmonary infarcts?
Prostatic hyperplasia

ANATOMICAL DIAGNOSES

Oat-cell carcinoma of lung, with metastases to regional lymph nodes, liver and cystic duct lymph nodes
Portal cirrhosis of liver
Chronic myocarditis, nonspecific

PATHOLOGICAL DISCUSSION

DR. SNIFFEN This patient was obese, with female hair distribution. We could not find a cause for the apparent intestinal obstruction. The stomach contained a 4-mm benign, peptic ulcer on the lesser curvature, 10 cm proximal to the pyloric ring. The prostate was small and did not contain cancer. The liver weighed over 2000 gm and had the gross and histologic appearance of portal cirrhosis. In addition, the parenchyma was studded with many 2- to 10-mm nodules of metastatic cancer, and a large lymph node containing metastatic carcinoma almost occluded the cystic duct.

The primary tumor was found in the left lung. It was only 1.5 cm in diameter and arose in the dorsal division of the lower lobe bronchus. Several satellite nodules of the same size were grouped around this tumor, which proved to be an oat-cell carcinoma. The hilar lymph nodes were not involved. The patient's heart was of normal weight, and there was disease in the coronary arteries. The myocardium, however, showed a patchy chronic myocarditis. The character of the inflammation was not specific, but it included giant cells. I should not consider this to be an important factor in the patient's death.

DR. RICHARDSON What about the bone marrow?

DR. SNIFFEN There were no metastases in the vertebral marrow.

DR. RICHARDSON Why did he have pain in the left arm and so forth?

DR. SNIFFEN I cannot explain that. We did not examine the veins of the extremities or the long bones.

DR. RICHARDSON Then I still have a loophole

DR. SNIFFEN This is one of the few cases we have seen of metastatic carcinoma in a cirrhotic liver. Reports vary concerning the frequency of its occurrence, some stating that it is rare, the cirrhosis protecting the liver from metastases, and others that the incidence is the same in both the cirrhotic and the noncirrhotic liver.

CASE 31492

PRESENTATION OF CASE

A forty-two-year-old man was admitted to the hospital complaining of paralysis of the left arm and leg.

Three weeks before admission he noted the onset of "tightness" in the neck and "light-headedness" without definite headache. These symptoms became more marked. Five days before admission he awoke complaining of weakness and numbness of the left hand and arm, which later in the day was followed by slight numbness and heaviness of the left leg. The numbness was described as a cold, dead feeling without tingling. On the evening of the same day he had a single generalized convulsion. The left hemiparesis progressed, and three days before admission the patient could not walk because of marked weakness of the left leg. The following day he was unable to move either the left arm or the left leg. Left facial weakness and ptosis appeared. At about the same time slowing of the mental processes was noted, and during the two days before admission he became increasingly lethargic. He never complained of nausea, vomiting, headache or visual or auditory disturbances. There was no history of head injury.

For a number of years he had had a slight cough, productive during the year before admission of a small amount of mucoid sputum. There was no hemoptysis, chest pain or weight loss.

Physical examination revealed the patient to be lethargic but oriented, at times he was comatose. The fundi were normal. The neck was slightly rigid. The lungs were dull to percussion throughout. The breath sounds were diminished over the entire right chest, those signs were most marked at the bases, where coarse rales were heard. The heart was slightly enlarged to percussion. The rhythm was regular except for an occasional extrasystole. The abdomen was moderately distended. There was a left homonymous hemianopsia. There was a left hemiplegia, the upper as well as the lower facial muscles were paralyzed, and the arm and leg were flaccid except for slight spasticity of the biceps. Sensation was impaired over the left half of the body, touch was not felt, pinprick was barely perceptible, and proprioceptive sense was lost. The arm, knee and ankle jerks were active, more so on the left than on the right. The plantar reflex was extensor on the left, and normal on the right.

I have here a long list of symptoms that I was going to try to explain, but I have talked enough. We have evidence that he had angina, and I believe some coronary sclerosis, but it does not seem to me probable that that was the cause of death or enters very much into the clinical picture. The dilatation of the bowel could perfectly well go with a sick liver in a malnourished man. It is frequently seen in pernicious anemia and in any nutritional disturbance. I do not believe that we have to postulate obstruction. A cecostomy was done and no obstruction demonstrated, as I understand it.

I am going to say that this man, besides having benign hypertrophy of the prostate, which is more or less historical, and a mild coronary sclerosis, had portal cirrhosis of the liver and peptic ulcer involving the duodenum and perhaps the stomach, and that he had nothing else. I think that perhaps he died a postoperative death for the reasons outlined.

DR J H MEANS I saw this man during the first part of his last admission, I did not witness the terminal events, because the service changed. We went through much the same diagnostic throes that Dr Richardson has. We were quite impressed by the fact that he had been orchidectomized and treated by stilbestrol. We could not be sure that there was any evidence that he had ever had carcinoma of the prostate. We also thought that the prostate had nothing to do with the picture. He was bleeding from the gastrointestinal tract and apparently had a large liver. I was not certain of the latter, but I think that the others who saw him were. I toyed with the idea of cancer of the stomach, perhaps with involvement of the liver, but I do not believe that the others were impressed with that possibility. At the time I left the service we established the diagnosis that he did have cirrhosis but it was described as an early one. I was not convinced that that was the only thing he had. He had an ulcer, and I thought that he might have a cancer as well.

DR RICHARDSON There is one other thing that I ought to mention. There has been some talk to the effect that stilbestrol is toxic to the liver. I believe that that has been disproved.

DR FLETCHER H COLBY I have not seen any evidence of toxicity when the drug has been given in large amounts for a long period of time.

I saw this man five years after his transurethral resection and three years after the orchidectomy. At that time, there was no evidence that he had cancer of the prostate. As we read over the history, we find that he had a transurethral removal of prostatic tissue, which had been examined and reported benign. That is not an infrequent occurrence in people who do have cancer of the prostate, because the most frequent place for cancer of the prostate is in the posterior lobe. In transurethral resection or subtotal prostatectomy, we do not remove any

of the tissue from the posterior lobe. So it is possible that he had cancer of the prostate limited to the posterior lobe of his gland. It is also a frequent occurrence in patients with cancer of the prostate who have had an orchidectomy performed that the regression of the tumor is so marked that on clinical examination no one can be certain whether the patient has cancer of the prostate. It is true that the regression is, in our experience, only temporary, lasting for a period of a few years. This man lived for three years after the orchidectomy and it still is possible that he had cancer of the prostate. He had also been treated with stilbestrol which causes regression of the primary tumor. I do not believe that anyone can say from the evidence presented in this history and examination whether or not the patient had cancer of the prostate.

DR EARL GLENDY To go back to the symptomatology, in the presence of pain in the chest that later radiated into the extremities, one should always think of some vascular accident, such as a dissecting aneurysm, but that usually occurs in persons with considerable evidence of hypertension. There is only one record of the blood pressure given in the protocol. Apparently little attention was paid to the blood pressure and the patient's cardiovascular status after the episode of pain in the chest and leg, so that I doubt that a dissecting aneurysm was present. It is another thing, however, that one should think of with pain radiating to the chest and to the lower extremities.

DR RICHARDSON It is fair to say that I thought of dissecting aneurysm and ruled it out particularly because the cases I know of, with dissection down to the iliac vessels, have had midback pain.

DR GLENDY The radiation of the pain is bizarre but the pain usually does not radiate into the arm which is another point against a dissecting aneurysm.

DR RICHARDSON I meant to add one other thing. I have to put a question mark after the thrombophlebitis, which I have already mentioned, and should also like to add pulmonary infarcts. I shall probably wish that I had not.

DR WADE VOLWILER I should like to say something in defense of the initial surgery. During one afternoon on the ward, this man began to complain of violent cramplike abdominal pain, and the previously distended abdomen became more distended and the normal peristalsis became high-pitched and quite typical of intestinal obstruction. He was taken to the X-ray Department, where a flat abdominal film demonstrated large dilated loops of colon including the ascending, the transverse and part of the descending colon, stopping abruptly in the sigmoid, which was compatible with obstruction of the sigmoid. On the basis of that, the original cecostomy was done. Unfortunately after the bowel was decompressed a barium enema was not done before the final surgical maneuver was carried out.

DR RICHARDSON I was not objecting to the

There are only two other significant vascular lesions that I want to consider — thrombosis and hemorrhage. Let us consider hemorrhage first. From the rapid course that this man followed and from the extensiveness of the lesions that he presented, it would seem that, if this were solely due to hemorrhage, one would have found red cells in the spinal fluid. Besides, the course was too long for hemorrhage, particularly for a large hemorrhage, which it would have to be in order to produce this picture. Cerebral hemorrhage usually comes on and ends in a much more abrupt manner. So that leaves me with just one other diagnosis, namely, thrombosis. This too, is usually a much more abrupt lesion. Furthermore, it is not ordinarily associated with convulsions. Convulsions and a relatively slow course are not unheard of, however, and if one had involvement of small arteries first and then large ones, it could produce this kind of clinical picture. Furthermore, when thrombosis does come slowly, one is apt to observe convulsions. When convulsions do occur in association with thrombosis, and it is not a rare phenomenon, they seem to come most frequently with occlusion of the middle cerebral artery.

In regard to localization, we know that a somewhat similar picture to this — that is, hemiparesis, hemianopsia and hemihyperesthesia — can be produced by thrombosis of the anterior choroidal artery. In such cases, however, weakness is not so pronounced, it is usually mild. Also little or no disturbance of consciousness is found. The ptosis noted in this case, I believe, was not associated with any involvement of the oculomotor nerve, such as in Weber's syndrome, but probably was due to weakness of the frontalis muscle. Therefore, I think that the lesion in this case was supratentorial, in the right cerebral hemisphere and probably in the distribution of the right cerebral artery. The pathologic process was probably thrombosis.

DR CHARLES S. KUBIK: The pupils reacted normally when the patient was admitted. The rectal temperature was 100°F, and the blood pressure 120.

Dr Porter, have you anything to add?

DR. HUNTINGTON PORTER: The only thing I should like to say is that I thought the sensory findings were dependable, since one could demonstrate good position sense and pain sense on the right side.

DR WILLIAM H. SWEET: The findings at operation were rather interesting. An enormous bone flap over the central region was turned down, disclosing a dura under extreme tension. I did not believe, as Dr Weisman did, that a rapidly growing tumor or an abscess could be ruled out positively on the basis of the clinical course. I thought that perhaps the most hopeful thing would be that he had a

slowly developing hemorrhage into a more or less benign tumor. At any rate it was with the hope of finding something of that sort that a craniotomy was carried out.

When the dura was reflected over the temporal lobe, grossly abnormal gyri were seen, and a ventricular puncture needle put into this portion of the temporal lobe fell through the substance of the brain by its own weight, indicating a gross area of softening. On direct inspection, we thought there might have been an area of diffuse cerebritis or an area of softening with vascular occlusion. The temporal lobe was removed in an attempt to remove the tentorial pressure cone.

DR AUGUSTUS ROSE: Would not the dilatation of the pupils and the coma suggest a pressure cone as the final cause of death?

DR WEISMAN: Yes.

DR KUBIK: You have in mind a temporal pressure cone as a cause of the dilatation of the right pupil?

DR ROSE: Yes.

CLINICAL DIAGNOSIS

Brain tumor

DR WEISMAN'S DIAGNOSES

Occlusion of right middle cerebral artery, probably due to thrombosis
Cerebral infarction

ANATOMICAL DIAGNOSES

Embolism of middle cerebral artery, right
Cerebral infarction

PATHOLOGICAL DISCUSSION

DR KUBIK: This was a difficult and puzzling case. It is unusual in cerebral infarction for the symptoms to progress gradually over so long a time or to have such a marked elevation of spinal-fluid pressure. Such pronounced coma as this patient eventually had, before he was operated on, is not frequent. Yet, the autopsy confirmed Dr Weisman's diagnosis.

There was an occlusion of the right middle cerebral artery, and softening of a large part of the right cerebral hemisphere. The vessel was occluded by an embolus, not by a thrombus, but no source for the embolus was found. There was some infiltration of the embolus with polymorphonuclear cells, which suggests an infectious process, and perhaps the possibility of an undiscovered or overlooked subacute bacterial endocarditis has to be considered. There were no infarcts in any of the other organs. There was a terminal bronchopneumonia. Examination of the lungs microscopically did not reveal any thrombosed lung veins, as a possible source of emboli.

Examination of the blood revealed a red-cell count of 5,080,000, with 14 gm of hemoglobin, and a white-cell count of 16,100, with 90 per cent neutrophils, many of which were band forms. The urine was normal. Lumbar puncture yielded clear, colorless fluid under an initial pressure equivalent to 310 mm of water. The cell count was 5 lymphocytes and 4 large mononuclears, no red cells were seen. The total spinal fluid protein was 46 mg per 100 cc, the sugar 116 mg. The gold-sol curve was 0011223110. Cultures of the fluid were negative.

An x-ray film of the chest showed a high diaphragm, but no evidence of pulmonary or cardiac disease. The skull, mastoid processes and sinuses were normal.

Shortly after admission, the patient sank into a deep coma. The right pupil, and later the left, became dilated and fixed to light. A craniotomy was done. The patient died six hours later or eleven hours after entry. The temperature had risen to 105.3°F, the pulse to 100, and the respirations to 60.

DIFFERENTIAL DIAGNOSIS

DR AVERY D WEISMAN In reviewing this case I should say that the sensory involvement ought to be considered in connection with the fact that the man was not alert. He was stuporous and at times comatose.

I think that this man's chest findings were probably due to pulmonary edema, with perhaps atelectasis.

Among the things that we do not have available in attempting to solve this problem of differential diagnosis are the temperature on entry, the blood pressure, the extraocular movements, the reaction of the pupils to light and the serologic findings.

Primarily one ought to consider an extracerebral lesion — subdural hematoma, for example. There was no history of head injury, but a good many people with subdural hematoma come into the hospital without such a history or the head injury is minor. Against subdural hematoma, however, is the absence of headache. Headache, especially unilateral headache, is often a symptom in subdural hematoma. Another point against it is that the hemiparesis appeared several days before the disturbance of consciousness. In most cases of subdural hematoma the reverse is true. The patient begins to get drowsy and toward the end develops weakness of the arm and leg. Another point against subdural hematoma is the complete left hemiplegia. When patients with subdural hematoma develop hemiparesis it is usually relatively mild. Still another point against it is the hemianopsia. I realize, however, that in a small percentage of cases of hematoma, hemianopsia is said to be present, but the figure is well under 5 per cent. When it is present, one wonders whether there is also an involvement of the posterior cerebral artery. I believe that subdural hematoma is the only significant extracerebral

lesion that one should consider, but I do not believe that that is what he had.

Thus we must think of some intracerebral lesion that can give this sort of picture. The first thing that comes to mind is a rapidly developing tumor, such as a metastatic tumor or, likelier, a glioblastoma, which as you know can sometimes appear so abruptly that it almost simulates a vascular accident. But it seems to me that the symptoms that this man presented were too widespread and too rapid — that is, the complete paralysis and the hemianopsia came on in too short a time — to be consistent with a brain tumor. In other words, this man within a few days developed weakness, severe paralysis of the arm, leg and face and also hemianopsia, and it is difficult to conceive of a glioblastoma, even one of the most malignant type, that would give this picture in such a short time. Furthermore, I should think that, were this the case, headaches would have been a more prominent part of the clinical picture.

One might also consider, among other intracerebral lesions, brain abscess. I might dispose of this possibility briefly by saying, first, that we have no idea where the abscess could have arisen and, second, that the course was too rapid even for an acute brain abscess. The acute brain abscesses that I have seen have all had a course of at least ten days. Also, if an abscess followed such a rapid course, one should have found more evidence of spinal-fluid abnormality on lumbar puncture.

We then come to other conditions, which seem likelier. The first one is central-nervous-system syphilis, because we know that neurosyphilis can often give paralysis and also a convulsion, which we note that this man had. But what kind of neurosyphilis could he have had? The most obvious one that comes to mind is general paresis, because that can occasionally produce a picture like this. I think, however, that the picture is exceedingly acute even for the most malignant type of general paresis. Furthermore, the spinal fluid should have been more abnormal than it was. The spinal-fluid protein was just on the borderline, as was the gold-sol curve and the cell count. Also, the pressure was elevated, which is not often seen in general paresis. It is seen, however, in syphilitic hydrocephalus, but that is an extremely rare condition. We do not know the serologic findings, which would tell us whether the patient had syphilis of the nervous system. As I have said before, we should like to know whether his eyes reacted to light, but even without that information I do not believe that this man had paresis. The other form of neurosyphilis to be considered is the meningovascular type. We know that that can often lead to situations that simulate or actually are vascular lesions. Again, in a man who ran such a rapidly lethal course I should expect more abnormalities than those which the lumbar puncture showed.

any possible exceptions to the rule, the lavish sampler might at least turn it over in his mind

DIABETIC NEUROPATHY

The article on diabetic neuropathy by the late Dr Abraham Rudy, published elsewhere in this issue of the *Journal*, deserves careful scrutiny. If his observations are properly interpreted and intelligently applied, many a diabetic man and woman will be lifted out of the "Slough of Despond," usually considered to be brought about by arteriosclerosis and old age, to a level where they can be studied, where their neuritis can be diagnosed and where their bodies can be rescued with good diabetic care.

Certain implications might be ascribed by the nonreflective reader to Dr Rudy's descriptions of a group of patients in whom the neuritis appeared to follow the inauguration of treatment. In several, it is true, the neuritis did come to light when treatment was begun, but careful reading of the text leads one to suspect that the neuropathy was present in latent form long before it was recognized by the patient or the physician. Indeed, one must concede that the symptoms and signs of diabetic neuropathy rarely develop following the beginning of diabetic treatment. Rundles¹ discusses this very point in a recent paper on diabetic neuropathy, stating that in only 16 per cent of 125 cases of diabetic neuropathy were symptoms of neuritis first noticed within two weeks after treatment was commenced. Diabetic neuropathy as a rule does not develop or progress when the diabetes is well controlled, in fact just the opposite is true. The term "well controlled," however, is not always properly employed. One is not justified in stating that a diabetic patient is well controlled if the urine is sugar free, and the blood sugar normal — altogether too many patients

of that type were seen in the days of undernutrition, and certain of them died. Control of diabetes means normal chemical tests along with mental and physical vigor and a reasonable body weight. These reflections, however, do not detract from Dr Rudy's paper, and hereafter the physician must look not alone for cancer and arteriosclerosis in every patient with diabetes whom he sees but also for symptoms, premonitory or existing, of neuropathy.

Rundles emphasizes that the increase of the total protein of the spinal fluid often observed in cases of diabetic neuropathy²⁻⁴ is an aid in differential diagnosis. On the other hand, some patients with severe diabetic neuropathy have a normal spinal fluid.

Important from the patient's point of view are the pathetic histories recounted by Dr Rudy. Months are usually required for recovery — a halting, painful progress back to health. Mental

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and sensory improvement often occurs earlier than does physical improvement. Indeed, one can almost safely say that the neuropathic patient will finally get well if he lives long enough; there is no royal road to recovery.

Dr Rudy has stated that there is "no direct relation between the duration or the severity of the diabetes and the presence of the neuropathy." It might be added that the development of neuritis in a case of mild and well treated diabetes of short duration is so unusual and spectacular that it always attracts more attention than it deserves. Rundles writes

Insofar as diabetic retinopathy and diabetic neuropathy coincide I have found an identical background of inadequate care extending over a considerable length of time preceding each complication. It will be apparent that few of our diabetics who developed neuropathy had received treatment meeting even these minimal standards and that the period of neglect had extended over a period of many months or years. None of this group [were] found to be among those regularly attending our diabetic

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OUT OF THE (GIFT) HORSE'S MOUTH

THERE is, in the drug detailing game, no particular time of year when the Christmas spirit seems especially appropriate, the wise men bearing gifts may appear at any season, on any working day and at any hour of the day, if the doctor is in. If they can buttonhole him for an impressive conference so much the better, if not, there appears upon the waiting-room table or the laboratory shelf the latest literature on the newest nose drop, vitamin combination, chemotherapeutic agent, antibiotic or what have you, with samples, frequently in quantity, despite the well known theory that the gift without the giver is bare.

One inference to be deduced is that the competition among drug manufacturers is too hot to handle, and another that the bags of the detail brigade are too heavy for the representatives of this friendly tribe to tote too long from door to door. In any event the situation poses a problem for the scrupulous physician in our frugal New England states, who is hard put to give away, as fast as they come in, those samples that his family cannot personally use. Being of New England stock, he hesitates to pitch out the unwanted bottles and boxes until he is sure that their contents are absolutely worthless, and being scrupulous, he cannot bring himself to sell those that might have value. And so his shelves grow fuller and fuller, to hastening pills a prey, as Dr. Goldsmith might have put it.

Advertising, we have been led to believe by the advertising fraternity, is good business, and so it must be, particularly in our amazing form of society where it is necessary to convince the public that it must have something that it has never heard of and has always done perfectly well without, in order that the wheels of industry may hum and that other workers, in turn, may earn the wherewithal to purchase similar products. It is difficult, nevertheless, to determine just what forms of advertising bear the best fruits, and it seems likely that the wholesale sowing of unsolicited drug samples must increase, to the ultimate consumer, the cost of these goods to an unwarrantable degree. A solicited sample is one thing; the advertising of it has been so well conceived or the product is of such potential merit that the solicitor's interest has been aroused and he takes the trouble to return the postcard. On the other hand, the stream of unsolicited samples that pours into the practitioner's office does little more, often, than to arouse in the doctor a feeling of frustration at his hopeless efforts to achieve and maintain any degree of orderliness.

Some astute aphorist at one time enunciated the doctrine that we get, in the main, what we pay for. This maxim was intended to give point to a general rule, with all its exceptions, not simply to declare a natural law that must remain immutable under all circumstances, like Boyle's law or the law of gravity or even, perhaps, the law of averages. Despite the

the extensive trips, with their whole equipment on their backs, he learned to live off the country. Because he had to meet all conditions of weather and travel without any of the artificial aids of civilization, he early learned that to live in any kind of comfort, in fact often even to live at all, it was essential to know and follow the laws of Nature. This was still further emphasized in his sailing days, for he was an ardent yachtsman. He not only rounded the New England coast himself but sailed as a Gloucester fisherman to the Grand Banks with Captain Bohlin, in the days when all dependence was on sail and the first boat in to the market with the money. It is perhaps from these outdoor contacts that he gained his uncanny ability to foretell weather and some of his often colorful and picturesque language. It certainly added to a physical ability far above that which generally accompanies one of his rather small stature.

Early in World War I his clear thinking led him to recognize that it was part of a world revolution and thus that the United States should participate, and with his fearless determination always to speak for the truth, he tried to mold public opinion. Naturally, he made enemies. Late one night he was attacked by three thugs apparently hired for the job. All of them were arraigned in court, but two only after they had been discharged from the hospital. After that, his friends ceased trying to have him carry a revolver for protection.

During the next few years in France he again had to call on his physical reserves, since he went for months with only three or four hours' sleep each night. He made an enviable record in the British Expeditionary Force and, because of this, was made a Commander of the Order of St. Michael and St. George. While in England he developed a close companionship with many of the surgeons at "Barts," a relation that persisted for the rest of his life.

At Ann Arbor, free from the tension of competitive practice, he devoted his full time to teaching and to the development of the medical school and hospital. He gathered around him a group of medical men, specialists in their respective fields, who, under his stimulating leadership, proceeded to build up what is today one of the great medical schools of this country. Here also his clear thinking carried him ahead of his contemporaries. Among other things, his insistence on full-time teachers and a large hospital for clinical facilities aroused opposition. Had he been a good politician during these years, being willing to give here or there, to compromise occasionally or at times even to refrain from speaking the obvious truth, he might well have finished his work at Ann Arbor. That, however, was not his way. He must say what he believed, often to stimulate discussion and to start thinking. This was understood by his friends, but often it only served to arouse more opposition among those

not accustomed to his ways. The latter did not realize that he was always willing to change his mind when shown that he was wrong, but he *must* be shown. So it was that he finally had to leave Ann Arbor.

For years he and Will Mayo had been friends, and he was at once invited to become a part of the Mayo Clinic. There, as professor of surgery, he continued his teaching, but only to graduate students. Always an inspiring teacher, he developed the seminar method to a high level. These seminars became famous throughout the country, and the exchange of ideas between students and faculty were valuable to both. No one who attended one of these sessions will forget the way in which he directed and co-ordinated the fullest discussion toward a definite end.

He had long been interested in the social and economic aspects of medicine, and during this period he began writing and speaking on this subject, which he continued to do the rest of his life. His first book, *The Doctor's Bill*, was published in 1936, and *The Patient's Dilemma* in 1940. His knowledge on the subject was extensive, and when he developed the beliefs that the evils of the present method of practice were harmful to both physician and patient and that they could be corrected to the advantage of both, he became a crusader for what he believed was the truth.

In 1939, in attempting to make a practical application of his ideas, he was one of the founders of the White Cross in Boston, a scheme for the complete prepayment of medical services. This aroused opposition among physicians but was slowly progressing when the war brought it to an end.

During his last few years, physical limitations did not prevent an active interest in current events in medicine and world affairs. He continued to lecture and to write, and his correspondence with persons in this country and England was extensive. His clear thinking and vigorously expressed opinions were unabated. His scorn of selfishness, of smallness and of low behavior in high places was not one whit diminished. His devotion to truth as he saw it was as strong as ever. His belief in a God of Law was with him always.

A great host of those who owe much to his stimulating teaching will mourn a great leader. Many of his contemporaries will miss a loyal friend. Those who loved him know that "Valiant-for-Truth" has passed over.

E L Y

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

GORAY—James P. Goray, M.D., of Fitchburg, died November 12. He was in his seventy-ninth year.

Dr. Goray received his degree from Harvard Medical School in 1891. He was a fellow of the American Medical Association.

clinic or under the adequate supervision of competent physicians with provision made for enlightened dietary management, frequent urinalyses, blood sugar determinations, when indicated, and checkup visits. In 25 cases there had been no diabetic treatment at all before the hospital admission. Of the remaining patients that had had some treatment, nearly every one (98 cases) had had what could be called "poor" care partly because of the obvious likelihood of failure.

Studies on the vitamin content of the diets of diabetic patients with and without neuropathy give little encouragement to the assumption that avitaminosis is the primary cause of this diabetic complication. In general it can be said that, if a true vitamin deficiency exists, a definite response should follow two weeks of adequate vitamin therapy. Deficiency states, however, are often so difficult to recognize that it is probably wise to give liberal doses of the various vitamins, including thiamine chloride, along with other therapeutic measures. Meanwhile, one should remember that this type of therapy is probably the least important of all the

things that are done to bring the diabetes under control and that one must wait for the diabetic neuropathy to disappear.

Although two of the late complications of diabetes—arteriosclerosis and diabetic cataracts, are irreversible once they become established, the early stages of diabetic neuropathy and of retinopathy are far more susceptible to treatment if it is carried on so rigorously that both the chemical and physical conditions of the patient are kept close to normal. Dr. Rudy's paper shows that even extreme cases of diabetic neuritis can be helped. This distressing complication can undoubtedly be cured in mild cases and can be averted in the majority of diabetic patients by prophylactic therapy.

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OBITUARY

HUGH CABOT

1872-1945

Hugh Cabot died a few days after his seventy-third birthday from a coronary attack, which was immediately fatal.

He was born in Beverly, Massachusetts, on August 11, 1872, one of seven brothers. He prepared for college at Roxbury Latin School and graduated from Harvard College in 1894. Four years later he graduated *cum laude* from Harvard Medical School, having stood second in his class. After completing his surgical internship at the Massachusetts General Hospital he began the private practice of surgery in Boston, at first as assistant to his uncle, Dr. Arthur Tracy Cabot.

His progress up the professional ladder at the Massachusetts General Hospital and at the Harvard Medical School was what would be expected. At the one he served consecutively as instructor, assistant professor and professor, and at the other, as out-patient surgeon, assistant surgeon and surgeon. His interest in urologic surgery was stimulated by that which his uncle had always taken in this branch, and largely because of this stimulus he organized the Department of Genitourinary Surgery at the Massachusetts General Hospital in 1910, with a clinic in the Out Patient Department and ten beds in the hospital.

In 1916 he went to France as head of the Harvard Unit, serving through the last of the war as a lieutenant colonel in the British Expeditionary Force in charge of Base Hospital No. 22.

Shortly after his return in 1920 he went to Ann Arbor as professor of surgery at the University of Michigan Medical School, and two years later he became dean. In 1930 he left Ann Arbor and went to Rochester, Minnesota, where he became a consultant and operating surgeon at the Mayo Clinic and professor of surgery at the Graduate School of the University of Minnesota Medical School. He held these positions until his retirement in 1938.

He married Mary Anderson Boit in September, 1902. She died at Rochester, Minnesota, in October, 1936. They had four children—three sons and a daughter. In October, 1938, he married Elizabeth Cole Amory. She and the three sons survive.

So much for the skeleton that gives only the framework of his life. What about the man? Three lines at the head of his Fiftieth Anniversary College Report may start the picture: "Eminent Surgeon and Medical Dean. Eloquent Speaker and Writer. Ardent Crusader in War and Peace, Brushing aside All Men and Things if They Block the Way to Truth."

Very early he became interested in the outdoors, first through his father, who was an excellent naturalist. With him he spent much time in the fields and woods in Brookline. When only thirteen he went with a guide into the Adirondacks. Three years later he was at the Maine woods then to New Brunswick, Quebec, Labrador, British Columbia and Alaska. For many years the vacation he loved best was to pick out some unmapped spot in the North Country with Tommy, his Indian guide, and to spend several weeks exploring. Dur-

the procurement of whole blood would greatly benefit the people of the Commonwealth

During my military mission to Moscow in 1943 I was really impressed by the fact that our Russian colleagues had valued the value of blood banks for their people years before the recent war began. We in our country, who should consider ourselves as enlightened in medical matters as the other peoples, must not now neglect the responsibility to see that all citizens have blood available in our hospitals when the occasion for its use arises

ELLIOTT C. CUTLER
BRIGADIER GENERAL, MC, A US

BOOK REVIEWS

The Story of a Country Medical College. A history of the clinical school of medicine and the Vermont Medical College, Woodstock, Vermont, 1827-1856. By Frederick C Waite, A M, Ph.D. 8°, cloth, 213 pp. with 8 illustrations and frontispiece. Montpelier Vermont Historical Society, 1945 \$4.50

This is the story of the medical college at Woodstock, Vermont—a proprietary school founded in 1826 by Dr. Joseph A. Gallup of Stonington, Connecticut, which lived bravely until it passed into desuetude in 1862.

Dr. Waite has done an immense amount of research in the book's creation. He describes medical education in the United States before 1826, traces the antecedents of the Woodstock school, gives a delightful description of Dr. Gallup and of how he happened to establish a medical school and, finally, tells how schools like this one became outmoded as cities grew, as means of communication advanced and, above all, as the belief became established that clinical teaching at the bedside is an essential part of medical education.

The Woodstock school filled a useful purpose in supplying doctors to its part of the world when they were badly needed. It started unpretentiously in the Eagle Hotel facing the Woodstock Common but presently moved westward into "a commodious brick building in a very eligible situation" on the edge of the village, it was twice married—to speak euphemistically—once to the Waterville College, of Maine, and once to Middlebury College, of Vermont. Neither union was felicitous, however, and so the school ended its days as independently as they were begun.

Besides writing a lively account of an interesting episode in the history of medical education, Dr. Waite has accomplished an exceptionally difficult task. He gives a complete record of everyone who had anything to do with the school—students, trustees and faculty, including a number of famous peripatetic professors, who they were, whence they came, and where and when they died. To collect authentic information of this character, obtained only with difficulty, represents particularly time-consuming and arduous effort.

The book is bound to appeal to all readers who enjoy learning of New England ways.

Cinchona in Java. The story of quinine. By Norman Taylor. With an introduction by Pieter Honig. 8°, cloth, 87 pp., illustrated. New York Greenberg, Publishers, 1945 \$2.50

Mr. Taylor is director of the Cinchona Products Institute in New York City. He has written an interesting popular account of the discovery of cinchona and its commercial development, particularly in Java, where the bulk of quinine used by the world is produced.

The natural habitat of the genus is along the Andes in South America, from Bolivia to Colombia, and the best wild bark comes from Bolivia, but the production from this territory does not equal the local demand. When it became evident that the South American bark production could not supply the world demand, the Dutch and English, as early as 1852, in the Netherlands Indies and in India, began attempts to cultivate cinchona trees.

The Java industry began in December, 1865, with the purchase of one pound of Ledger seed gathered in Bolivia. This species is now known botanically as *Cinchona ledgeriana*, and most of the commercial plantations in Java today consist of Ledger grafts on *C. succirubra* stocks. *C. ledgeriana*, although high in quinine, is low in the other alkaloids, whereas, *C. succirubra*, low in quinine, is high in quinidine,

cinchonine and cinchonidine. Plantations of the two species in Java now supply practically all quinine and cinchona alkaloids.

C. ledgeriana is difficult to grow, but *C. succirubra* is easily cultivated. Horticulturally, the problem was solved by grafting clones of *C. ledgeriana* on stocks of *C. succirubra*, the resulting trees supply the present world demand for quinine. Proper growth requires certain climatic conditions, and the trees do best at elevations ranging between three and seven thousand feet. The hills and mountains of Java furnish ideal situations. The real harvest from a plantation does not come until the trees are fifteen to eighteen years old, at that time they have reached full vigor and the bark is thick enough to cut profitably, the quinine content being at its peak. The plantation is then destroyed. The growers must keep a constant succession of planting from seed every year to ensure an adequate supply of quinine for the world.

The book is interesting and well written and should be in all libraries, public and medical.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Manual of Tropical Medicine. Prepared under the auspices of the Division of Medical Sciences, National Research Council. 8°, cloth, 727 pp., with 284 illustrations. Philadelphia W. B. Saunders Company, 1945 \$6.00

In this new book the contributors have endeavored to write a concise statement of the most recent available and authoritative information concerning the more important tropical diseases. Particular attention has been devoted to the epidemiology and the control of the communicable diseases of the tropics, and the most recent information concerning the therapy of these diseases has been incorporated in the text. The book is designed for use in the field, as well as in laboratories and schools and should serve as a convenient summary for public-health workers, epidemiologists and parasitologists. Some of the information on the incidence and transmission of disease in the tropics is original and hitherto unpublished. Considerable space has been devoted to medical entomology, and the illustrations in this section are morphologically accurate and should prove useful in the identification of parasites. This book should be in all medical libraries and in the libraries of physicians who come into contact with tropical diseases. It is issued as one of the series of military medical manuals sponsored by the National Research Council.

Clinical Roentgenology of the Digestive Tract. By Maurice Feldman, M.D., assistant professor of gastroenterology, University of Maryland assistant in gastroenterology, Mercy Hospital, and consulting roentgenologist, Sinai Hospital, Baltimore. Second edition. 8°, cloth, 769 pp., with 551 illustrations. Baltimore Williams and Wilkins Company, 1945 \$7.00

In this second edition of a special treatise, first published in 1938, the author has made the necessary changes to bring the material up to date. The book has been revised, rewritten and shortened to eliminate all unessential data, and many chapters and illustrations have been added.

Neuro-Ophthalmology. By Donald J. Lyle, M.D. lecturer on neuro-ophthalmology, Department of Anatomy Medical College of the University of Cincinnati and attending ophthalmologist to the Good Samaritan Hospital, Christ Hospital, Jewish Hospital, St. Mary's Hospital and Children's Hospital. 4°, cloth, 395 pp., with 234 illustrations. Springfield, Illinois Charles C. Thomas, 1945 \$10.50

The plan of this book is to bring together in a brief comprehensive and co-ordinated manner, those many phases of

MORRISON — William H. Morrison, M.D., of Springfield, died November 22. He was in his sixty-sixth year.

Dr. Morrison received his degree from Baltimore Medical College in 1905.

His widow, a son, a brother and a sister survive.

VANCE — Michael E. Vance, M.D., formerly of North Attleboro, died May 5. He was in his seventy-sixth year.

Dr. Vance received his degree from New York University Medical College in 1895. He was a member of the Rhode Island Medical Society, Pawtucket Medical Association, Attleboro Doctors' Association and a fellow of the American Medical Association.

His widow survives.

WARREN — Alva H. Warren, M.D., of Malden, died November 19. He was in his seventy-second year.

Dr. Warren received his degree from Harvard Medical School in 1900. He was a member of the New England Roentgen Ray Society and the American College of Radiology.

His widow, a daughter and a grandson survive.

WOODS — Charles E. Woods, M.D., of Fitchburg, died October 12. He was in his eighty-third year.

Dr. Woods received his degree from Dartmouth Medical School, Hanover, New Hampshire, in 1890. He was a past president of the Worcester North District Medical Society, and was the Lunenburg school physician from 1906 to 1941, when he retired from practice.

His widow, a son, a daughter and four grandchildren survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR OCTOBER, 1945

RÉSUMÉ

DISEASES	OCTOBER 1945	OCTOBER 1944	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	136	99	21
Chancroid	1	1	*
Chicken pox	331	370	390
Diphtheria	17	19	18
Dog bite	764	842	823
Dysentery, bacillary	39	32	32
German measles	46	35	35
Gonorrhea	657	438	416
Granuloma inguinale	0	0	*
Lymphogranuloma venereum	2	1	*
Malaria	38	36	0
Measles	648	274	373
Meningitis meningococcal	12	20	8
Meningitis Pfeiffer bacillus	2	4	2†
Meningitis pneumococcal	0	2	0†
Meningitis staphylococcal	0	0	0†
Meningitis streptococcal	2	0	0†
Meningitis other forms	3	2	4†
Meningitis, undetermined			
Mumps	326	350	204
Pneumonia lobar	96	159	192
Salmonella infections	5	15	6
Scarlet fever	372	456	458
Syphilis	436	408	408
Tuberculosis pulmonary	263	230	232
Tuberculosis other forms	23	16	29
Typhoid fever	3	1	4
Undulant fever	7	2	4
Whooping cough	638	286	375

*Made reportable December, 1943

†Four year average

COMMENT

Anterior poliomyelitis cases declined during October, which is similar to the seasonal fluctuation which has been observed in previous years. There were 136 cases reported for the month, as compared with 163 during September. A further and more marked decrease can be expected in the ensuing months.

Whooping cough was more than twice as prevalent during October as it was during the same month last year and exceeded the seven-year median for October by 70 per cent.

Measles cases also markedly exceeded those reported during October, 1944, being a little less than twice as high as the seven-year median.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Actinomycosis was reported from West Springfield, total, 1.

Anterior poliomyelitis was reported from Belmont, Beverly, 1, Billerica, 1, Boston, 22, Brockton, 2, Brookline, 2, Cambridge, 2, Chelsea, 3, Clinton, 1, Colrain, 2, Dalton, 4, Danvers, 1, Dartmouth, 1, Dedham, 1, Everett, 5, Fitchburg, 1, Framingham, 1, Framingham, 1, Grafton, 1, Haverhill, 1, Hingham, 2, Hopkinton, 1, Lancaster, 1, Lawrence, 2, Lenox, 1, Leominster, 1, Lexington, 1, Lowell, 2, Lynn, 1, Malden, 3, Medford, 11, Milford, 1, Millbury, 1, Milton, 4, Newton, 8, North Andover, 1, Northampton, 1, Norwood, 1, Orleans, 2, Pittsfield, 1, Quincy, 6, Reading, 4, Rochester, 1, Rockland, 2, Saugus, 1, Sharon, 1, Somerville, 3, Sutton, 1, Taunton, 1, Tisbury, 1, Walpole, 1, Waltham, 1, Watertown, 1, Wellesley, 2, Whitman, 1, Winthrop, 1, Woburn, 1, Worcester, 2, total, 136.

Diphtheria was reported from Boston, 2, Chicopee, 1, Cushing General Hospital, 1, Easton, 1, Gloucester, 1, Lynn, 1, Springfield, 3, Taunton, 1, West Springfield, 1, Worcester, 1, total, 17.

Dysentery, amebic, was reported from Camp Edwards, total, 2.

Dysentery, bacillary, was reported from Boston, 1, Cambridge, 3, Foxboro (State Hospital), 1, Lowell, 1, Malden, 1, Newton, 1, Peabody, 2, Worcester (State Hospital), 2, total, 39.

Encephalitis, infectious, was reported from Barre, 1, Pittsfield, 2, total, 3.

Hookworm was reported from Camp Edwards, 3, total, 3.

Malaria was reported from Boston, 6, Brookline, 1, Cambridge, 2, Camp Edwards, 13, Holbrook, 1, Medford, 1, New Bedford, 1, Newton, 1, Northboro, 1, Peabody, 1, Quincy, 1, Raynham, 1, Swampscott, 1, Waltham Regional Hospital, 4, Winchester, 1, Worcester, 2, total, 38.

Meningitis, meningococcal, was reported from Boston, 1, Camp Myles Standish, 1, Framingham, 1, Hanover, 1, Lowell, 1, Malden, 2, Quincy, 1, Springfield, 1, Westboro, 1, Wilbraham, 1, total, 12.

Meningitis, Pfeiffer bacillus, was reported from Huntingdon, 1, Somerville, 1, total, 2.

Meningitis, streptococcal, was reported from Randolph, 1, Winthrop, 1, total, 2.

Meningitis, other forms, was reported from Boston, 1, New Bedford, 1, total, 2.

Meningitis, undetermined, was reported from Cambridge, 1, Somerville, 1, Springfield, 1, total, 3.

Salmonella infections were reported from Boston, 1, Cambridge, 1, Dedham, 1, Ludlow, 1, Malden, 1, total, 5.

Septic sore throat was reported from Amesbury, 1, Attleboro, 2, Boston, 7, Camp Edwards, 1, Greenfield, 1, Merrimack, 1, Worcester, 1, total, 14.

Typhoid fever was reported from Attleboro, 1, Boston, 1, Salem, 1, total, 3.

Undulant fever was reported from Camp Edwards, 1, Hardwick, 1, Northampton, 1, Uxbridge, 1, Westboro, 1, Williamstown, 1, Worcester, 1, total, 7.

CORRESPONDENCE

VALUE OF BLOOD AND ITS DERIVATIVES IN CIVILIAN HOSPITALS

To the Editor: I have read the editorial on blood and blood derivatives in the October 4 issue of the *Journal* and should like to express my approval of any plan which makes easily available the use of blood in the hospitals of the Commonwealth for the good of the people. Experience in every theater of war during the last three years has built up an imposing weight of evidence that whole blood is an essential factor in the restoration of those who have lost blood to a satisfactory and safe condition. It is generally accepted that plasma alone is not an adequate substitute for whole blood when the problem is one of blood loss and a replacement of blood volume. Any mechanism which can be brought forward to continue the flow of donors to hospitals and centers

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OCCUPATIONAL DERMATOSES: DISABILITY AND COMPENSATION*

C. GUY LANE, M.D.†

BOSTON

DISEASES of the skin comprise 65 per cent of all occupational disease. There is, however, surprisingly little material indicating the actual amount of disability that occurs in these cases, the expense in terms of compensation paid or the medical costs involved. Compensation laws have been enacted in almost all the states, and it can be expected that such studies will be available later. These laws and the progress made since the original compensation act passed in Wisconsin in 1911 have been discussed by Foerster.¹ He points out that within fourteen years there occurred in that state three times as many compensable cases in the last year of the period as in the first year. Furthermore, in the last year, the expenditure for indemnity had increased six times, and the medical expenditures ten times. It is reasonable to suppose that occupational dermatoses have increased in a like measure, with similar increases in disability and compensation figures.

Industrial accidents are, of course, far more numerous than occupational diseases and provide many more serious cases. The study of these surgical cases has led to the development of effective methods of prevention and treatment, whereas occupational diseases, with their large proportion of cutaneous cases, have been relatively neglected. True, great advances have been made in the control of lead poisoning, silicosis and a few other serious conditions. On the other hand, the toll that cutaneous disturbances take in the occupational field is large and deserves more study than it has thus far received.

A search has been made for data that support this statement of losses, but there is to be found in the medical literature little evidence of the actual losses by disability, and only a few statements of the costs in connection with cases of occupational dermatoses. Insurance companies and state accident commissions do not have readily available the data on these items. Some commissions in their annual reports present figures, but this occurs

in only a few states, and no commission can register all the cases occurring in its state.

An attempt has been made to obtain recent figures concerning four items in connection with cases of disability due to occupational cutaneous disease: compensation paid during disability, medical expenses, amount of wages lost and the duration of disability or of time lost from work. The purpose of this paper is to present the data thus obtained and to discuss, with the hope of eventually reducing such losses, the criteria for the diagnosis of occupational dermatoses and the contributing factors of long continued disability.

Disability compensation and medical expenses, together with lump-sum settlements and the like, represent the total cost, but they do not include the wages lost. This loss is to a certain extent offset by the compensation, but the latter alone does not maintain the worker and his family as before, and such loss to the family is difficult to calculate. The time lost by a skilled worker also often represents a real loss to the employer, which is difficult to measure in dollars and cents.

In reviewing these data, it is recognized that a large number of workers with occupational dermatoses have no disability, or disability for an extremely short period. The number of these minor cases and the duration of disability of the major cases could be substantially lessened through better methods of early detection, correct diagnosis and insistence on adequate and proper treatment. This would obviate a large amount of time now lost from overtreatment and from secondary infection.

In contrast to the minor cases there occur from time to time long-drawn-out disabilities that are extremely costly to the employer, the employee and the insurance company. Blaisdell² cites 3 of these. In one, a shoe stitcher with minor disturbances on the hands was disabled for sixty weeks. The total compensation was \$567.00, the medical fees were \$112.00, and the total cost to the insurer was \$864.00. In another case, a shoe laster received for ninety-six weeks of total disability and thirty-four weeks of partial disability compensation totaling \$1902.57 and a lump-sum settlement of \$457.00. Medical

*Presented at the Mid West Clinical Meeting, Omaha, Nebraska, October 14, 1944.

†Professor of dermatology, Harvard Medical School, chief, Department of Dermatology, Massachusetts General Hospital.

neurology in so far as they concern, directly or indirectly, neuro-ophthalmology. The book is well illustrated, and an extensive bibliography is appended to the text.

Microbial Antagonisms and Antibiotic Substances By Selman A. Waksman, B.S., M.S., Ph.D., professor of microbiology, Rutgers University, and microbiologist, New Jersey Agricultural Experiment Station. 8°, cloth, 350 pp., with frontispiece. New York: The Commonwealth Fund, 1945. \$3.75.

This special monograph discusses the broad interrelations among micro-organisms living in association, either in simple mixed cultures or in complex natural populations, with special attention to the antagonistic effects. Emphasis is laid on the significance of these associations in natural processes and on their relation to disease production in man and in domesticated plants and animals. The chemical nature of the active antibiotic substances produced by various antagonists is described, and the nature of the antagonistic action, as well as its utilization for the practical use of disease control, is discussed. An extensive bibliography will be found at the end of the volume. This volume is recommended as a reference text for medical libraries and meets the previous high standard of Commonwealth Fund publications.

Medical Gynecology By James C. Janney, M.D., assistant professor of gynecology, Boston University School of Medicine. 8°, cloth, 389 pp., with 97 illustrations. Philadelphia: W. B. Saunders Company, 1945. \$5.00.

The scope of this book is limited to office gynecology and it has two aims: to aid the medical student in correlating didactic lectures with the experience obtained in the gynecologic clinic and to provide refresher material for the practitioner. The work is based largely on the author's experience in the clinical teaching of gynecology, and the general outline is the same as the course he gives in which he approaches the subject from the direction of the patient's complaints. Under the heading of sociomedical problems in gynecology will be found a chapter on marital maladjustments.

The Control of Communicable Diseases. An official report of the American Public Health Association. Sixth edition. 12°, paper, 149 pp. New York: American Public Health Association, 1945. 35 cents.

In 1917 a committee of the Health Officers' Section of the American Public Health Association first issued this small manual on standard regulations for the administrative control of the communicable diseases for which notification is usually required by state and municipal health authorities throughout the United States. This new edition has been revised and officially approved by the American Public Health Association and is official with the United States Public Health Service and the United States Navy, and has been approved in principle by the Surgeon General of the United States Army. The various diseases are arranged alphabetically and each disease is briefly described regarding its clinical and laboratory recognition, the etiologic agent, the source of infection, the mode of transmission, the incubation period, the period of communicability, susceptibility and immunity and the prevalence of the disease. Following this, methods of control affecting both the individual and the general population are described. Inasmuch as the legal phraseology necessary for formal regulations differ in each state, such regulations are not included in the text. This manual should prove useful to all physicians coming in contact with communicable diseases.

NOTICES

ANNOUNCEMENTS

Dr. Archie A. Abrams has resumed the practice of gynecology and obstetrics at 475 Commonwealth Avenue, Boston.

Dr. Marshall K. Bartlett, having returned from military service, is resuming the practice of surgery at 264 Beacon Street, Boston.

Dr. Theodore B. Bayles, having returned from service with the United States Army, announces the reopening of his office at 372 Marlborough Street, Boston, for the practice of internal medicine.

Dr. Emmanuel Deutsch is resuming his practice at 469 Beacon Street, Boston.

Dr. Sydney Ellis has resumed his practice of obstetrics and gynecology at 311 Commonwealth Avenue, Boston.

Dr. James Andre Lamphier, having returned to civilian practice, announces the opening of his office in the Professional Building, 270 Commonwealth Avenue, Boston, for the practice of obstetrics and gynecology.

Dr. Samuel S. Levinson, having returned from active service with the United States Army, has resumed the practice of general surgery at 483 Beacon Street, Boston.

Dr. Julius Loman announces the removal of his office to 483 Beacon Street, Boston.

Dr. Charles L. Short announces the reopening of his office at 264 Beacon Street, Boston, for the practice of internal medicine, with a particular interest in arthritis.

Dr. John W. Strieder announces that Dr. Joseph P. Lynch will be associated with him in the practice of thoracic surgery at 171 Bay State Road, Boston.

Dr. Fred F. Weiner is resuming the practice of urology at 231 Main Street, Brockton.

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, December 18, at twelve noon. Dr. Theodore L. Badger will speak on the subject "Medical Perambulations through Ireland, England and France." Dr. A. J. Clegg will preside. Physicians are cordially invited to attend.

VAN METER PRIZE AWARD

The American Association for the Study of Goiter again offers the Van Meter Prize Award of three hundred dollars and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland. Provided essays of sufficient merit are presented in competition, the award will be made at the annual meeting of the association, which will be held in Chicago in April or May, 1946.

The competing essays may cover either clinical or research investigations, should not exceed three thousand words in length and must be presented in English, a typewritten double-spaced copy should be sent to the corresponding secretary, Dr. T. C. Davison, 207 Doctors Building, Atlanta 3, Georgia, not later than February 20, 1946. The committee that will review the manuscripts is composed of men well qualified to judge the merits of the competing essays.

A place will be reserved on the program of the annual meeting for presentation of the winning essay by the author if it is possible for him to attend. The essay will be published in the *Proceedings* of the association. This will not prevent its further publication, however, in any journal selected by the author.

(Notices continued on page xvii)

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OCCUPATIONAL DERMATOSES DISABILITY AND COMPENSATION*

C GUY LANE, M D †

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Industrial accidents are, of course, far more numerous than occupational diseases and provide many more serious cases. The study of these surgical cases has led to the development of effective methods of prevention and treatment, whereas occupational diseases, with their large proportion of cutaneous cases, have been relatively neglected. True, great advances have been made in the control of lead poisoning, silicosis and a few other serious conditions. On the other hand, the toll that cutaneous disturbances take in the occupational field is large and deserves more study than it has thus far received.

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†Professor of Dermatology, Harvard Medical School; chief, Department of Dermatology, Massachusetts General Hospital.

care cost \$165 00, and the cost to the insurer was \$2680 00. In the third case, a shoe ironer with a constantly recurring dermatitis received for nearly seven and a half years a weekly compensation of \$11 83. The payment automatically stopped when they reached the full amount allowed by the law, \$4500. Medical care and other costs amounted to \$1000. There could well be some doubt, at least from the dermatologic standpoint regarding the validity of some of the recurrences suffered by this patient.

In a case from another source, a disability of more than forty-eight weeks resulted from a dermatitis and its complications, with total medical expenses of \$565 00 and a total compensation cost, including a lump-sum settlement, of \$1588 00. The wages lost were \$864 00.

The industrial-accident commissions of three states, Wisconsin, New York and Ohio, have been able to furnish data on the losses in protracted disability cases. The recent reports of the Industrial Commission of Wisconsin (Table 1) are of interest

were awarded a total of 14,605 weeks of compensation, with an average of 9.2 weeks (Table 3). The total compensation awarded was \$222,311 00, with an average of \$131 00. (It would be interesting to know whether the costs in Wisconsin and New York were computed on the same basis.) If the lost time in the temporary-disability group is increased by that in the cases with less than thirty-five days lost, in which no compensation was paid for the first week, the total amounts to 13,311 weeks. The wage loss in this group of cases has been estimated as \$160,000. Information concerning the amount of medical expenses incurred is not available.

A report by the Industrial Commission of Ohio gives no information regarding compensation paid or the medical expenses of occupational dermatoses, but furnishes data concerning the time lost in 1943. Of 4711 cases encountered during that year, 2 of which had a fatal outcome and 1 permanent partial disability, there was disability of over seven days in 780 and of seven days or less in 370, no

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	NO OF CASES TEMPORARY DISABILITY	CASES PERMANENT DISABILITY	NO OF DAYS LOST	AMOUNT OF INDEMNITY PAID	COST OF MEDICAL CARE	TOTAL COSTS
1941						
Dermatitis	359		6 686	\$17 153	\$12 114	\$29,267
Plant poisoning	182		2 123	4 078	3,450	7 528
Totals	541		8 809	\$21,231	\$15 564	\$36,795
1942						
Dermatitis	560	1	8 863	\$22 628	\$16 655	\$39 283
Plant poisoning	134		1 602	3,754	2 596	6 350
Totals	694	1	10 465	\$26 382	\$19 251	\$45,633

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TABLE 2 *Average Number of Days Lost and Average Indemnity and Cost of Medical Care in Cases of Dermatoses in Wisconsin (1937-1942)*

DATA	1937	1938	1939	1940	1941	1942
Average days lost	23	24	23	19	19	16
Average indemnity	\$53 00	\$60 00	\$61 00	\$48 00	\$48 00	\$40 00
Average cost of medical care	\$37 00	\$37 00	\$46 00	\$35 00	\$35 00	\$31 00

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non paid and medical expenses between January 1, 1940, and October 1, 1944. The total expense to the company was \$94,578.00. The average amount of compensation paid was \$76.00 and the average cost of medical expense was \$49.00, making the

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TABLE 3 Compensation for Cases of Occupational Dermatoses in New York State (1945)

TYPE OF CASE	NO. OF CASES	DURATION OF COMPENSATION		COMPENSATION AWARDED	
		TOTAL \$ ^k	AVERAGE \$ ^k	TOTAL	AVERAGE
Fatal	1	1 000	1 000 0	\$10 403.00	\$10 403.00
Partial disability	47	1,336	28.4	22 856.00	486.00
Temporary disability	1 652	12 269	7.4	189 052.00	114.00
Totals	1 700	14 605		\$222 311.00	
Averages			8.6		\$130.77

average expense per case \$125.00. If the cases in which no compensation was paid are deducted, the average compensation paid per case rises to \$94.00 and the average medical expense to \$52.00. The increase in the number of cases this year in the ten months of the year is especially striking, but there is no information concerning the large increase in the number of cases in which no compensation

lessen such losses.

Much has been written concerning the causes of disability and concerning hazardous occupations so far as occupational cutaneous disease is concerned, but it is not generally realized in what a high percentage of the cutaneous cases seen by the average physician a causal occupational factor arises. If all persons, including housewives, using

TABLE 4 Data in 753 Cases of Dermatitis (1940-1944)

YEAR	NO. OF CASES	COMPENSATION PAID	CASES WITH NO COMPENSATION	MEDICAL EXPENSES PAID	CASES WITH MEDICAL EXPENSE OVER		
					NO. OF	\$500.00	\$1 000.00
1940	20*	\$1 705	5	\$1 985	2	0	0
1941	65	9 726	9	3 947	6	6	2
1942	176	10 795	27	8 575	7	3	1
1943	174	13 526	27	8 954	12	7	2
1944	318*	21 720	75	13 642	21	6	1
Totals	753	\$57 472	143	\$37 106	48	22	6

*Incomplete figure.

was paid. There were only 6 cases in which the total expense was over \$1000.00, the largest amounting to \$3515. No data concerning duration of disability or wages lost were available.

Undoubtedly further effort would reveal other figures of similar nature. Other states were approached as well as other insurance companies, but the data were not readily available. There are thus very few figures indicating the medical expenses and compensation paid for these cases. There are even fewer data on the duration of disability and the amount of wages lost. There is only an occasional reference to the end results, that is, the ability to return to the same job or the need for transfer to some other job.

These extremely incomplete figures on duration of disability, wages lost, medical expenses and compensation paid for occupational dermatoses are impressive enough to warrant more attention by manufacturers, insurance companies and state accident commissions. Further studies should be made in an effort to determine the actual losses

soap and water in their work were considered, an occupational factor would need to be reviewed in 15 to 20 per cent of all dermatologic cases. It is therefore important for the physician to have in mind the criteria by which he is to determine the correct occupational liability. The National Committee on Occupational Dermatoses after much discussion made a report on this subject, which was published in 1942.³ The use of the criteria given in this report would be a distinct aid in the recognition of occupational cases, at least from the medical standpoint. In making decisions regarding the liability for disability from occupational dermatoses, the physician should answer the following questions, which are based on these criteria:

Has the patient been in contact with an agent known to have produced similar changes in the skin?

Is the time between exposure to the agent claimed and the onset of disease correct for that particular agent and for the particular disease that the patient presents?

Is the place on the body where the disease began the site where the greatest exposure has occurred?

Is the site of the greatest skin involvement the place where the greatest exposure has occurred?

care cost \$165 00, and the cost to the insurer was \$2680 00. In the third case, a shoe ironer with a constantly recurring dermatitis received for nearly seven and a half years a weekly compensation of \$11 83. The payment automatically stopped when they reached the full amount allowed by the law, \$4500. Medical care and other costs amounted to \$1000. There could well be some doubt, at least from the dermatologic standpoint regarding the validity of some of the recurrences suffered by this patient.

In a case from another source, a disability of more than forty-eight weeks resulted from a dermatitis and its complications, with total medical expenses of \$565 00 and a total compensation cost, including a lump-sum settlement, of \$1588 00. The wages lost were \$864 00.

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1940	20*	\$1,705	5	\$1,988	2	0
1941	65	9,726	9	3,947	6	2
1942	176	10,795	27	8,575	7	1
1943	174	13,526	27	8,954	12	2
1944	318*	21,720	75	13,642	21	1
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Has the patient been in contact with an agent known to have produced similar changes in the skin?

Is the time between exposure to the agent claimed and the onset of disease correct for that particular agent and for the particular disease that the patient presents?

Is the place on the body where the disease began the site where the greatest exposure has occurred?

Is the site of the greatest skin involvement the place where the greatest exposure has occurred?

- Are the lesions present consistent with those known to have followed a similar exposure or trauma?
- Is the person employed in an occupation in which similar cases have occurred?
- Do any of the other workers at the same job have similar manifestations on the skin due to the same cause?
- If the diagnosis is one of dermatitis, have attacks occurred after exposure to the agent claimed, and has relief occurred after cessation of exposure?
- If the diagnosis is one of dermatitis, and skin tests have been done by a generally accepted technic and interpreted by a competent physician, are the results consistent with the facts obtained from the history and physical examination?
- Is the diagnosis that of a disease in which a causal factor due to occupation has been established beyond reasonable doubt?
- Has the patient been exposed outside his work to an agent that might have caused a similar eruption?
- Is there any doubt concerning the diagnosis?

The two most influential factors that increase the difficulty of making a diagnosis and of determining the liability of occupational dermatoses are the length of time that has elapsed from the onset until examination and the failure to obtain an accurate history of the early period of the eruption. If the cases can be examined early and the satisfactory fulfillment of the criteria obtained, a definite diagnosis of occupational liability can be made. If the essential items of the criteria do not apply fully, all that can be said of a particular case is that it is *probably* one of occupational dermatosis. In numerous cases the only statement that can be made is that the case is of *possible* occupational origin, in other words, a reasonable or more than reasonable doubt exists of the industrial causation. For example, if the answers to the first ten questions are in the affirmative, the skin disturbance is undoubtedly occupational. If the answers to the last two questions are in the affirmative, there is reasonable doubt that occupational liability exists.

The most frequent diagnosis in patients incurring disability or receiving compensation for cutaneous disturbances is dermatitis venenata or contact dermatitis, but there are various other diagnoses in which consideration must be given to the occupational liability. As I⁴ have previously stated, the most frequent diseases in which an occupational factor can occur are as follows

NONINFECTIOUS DISEASES	INFECTIOUS DISEASES
Acne	Actinomycosis
Burns	Anthrax
Calluses	Blastomycosis
Chilblains	Erysipeloid
Dermatitis, acute or chronic	Impetigo
Eczema	Paronychia
Epithelioma	Pus infections
Folliculitis	Syphilis
Keloids	Tinea
Keratoses	Tuberculosis
Radiodermatitis	
Ulcers	

There are many other diseases in which an occupational factor may be a cause. It is to be remembered that in some states the complications of occupational disease and the effect of pre-existing disease in enhancing disability are also compensable.

This broadens the scope of the compensation laws, especially when all the possible complications of therapy are considered. The record of a diagnosis should include the fact that the dermatosis is occupational and should state the type of disease present (dermatitis, keloid and so forth), the cause (if known) and the occupation. With these data cross-filed, a study of various series of cases at a later period with reference to disability and compensation is an easy matter.

The type of disability that results from cutaneous disease is fully as varied as that in disease of any other organ. Most patients suffer a temporary disability, and many suffer a total disability for a shorter or longer period. A few are permanently disabled, in that they are unable to return to their jobs or must give up working altogether.

An occasional death occurs as the result of some complicating factor. Some patients have a partial disability in that they are slowed up in their work or can do only part of it or are limited to part-time work. An occasional permanent partial disability occurs.

The duration of the disability has many contributing factors. The most hazardous agents and the occupations in which the majority of cases occur have been discussed in numerous reports, and much preventive work for such occupations has already been outlined.⁵ Carelessness on the part of the worker or his failure to observe the preventive regulations concerning a particular product are often fundamental causes of a long disability, and in many cases deliberate failure to report an eruption for fear of losing time or for some other reason has caused a longer disability than would otherwise have resulted. Failure to detect cases early, whether on the part of the foreman, the nurse or the physician, is also a contributing factor. Additional exposure after the onset of irritation and the late commencement of treatment are extremely important in the prolongation of disability. Failure to have troublesome cases examined early by a physician with some training in cutaneous medicine is responsible for many cases of excessive disability. In a series of 40 shoeworkers studied, it was found that the average period before examination by a dermatologist was five weeks. The longest period was two years, and several cases were allowed to go for four to six months before having the possible benefit of more experienced advice.

It is also necessary to be sure that the worker is not suffering from a nonoccupational disease, such as erythema multiforme or lichen planus. Self-medication, usually of the wrong type, often contributes to extra disability. The use of an agent too strong for the skin adds its share to the toll. Sensitization of the patient, either to substances that he contacts during work or to agents used in therapy, occurs in a far larger proportion of occupational cases than is generally believed and may

add materially to the period of disability. Finally, secondary infection of a wound or a dermatitis may increase the time lost from work.

The cases with long disability that have been mentioned, as well as the two deaths mentioned by the New York report, are unusual, but they emphasize the possibility of long-continued disability and of high costs of an occupational dermatosis. Although only a limited number of figures regarding time and money lost from disability due to occupational dermatoses are available, these suggest that a further study should be made to ascertain the actual amount of loss incurred from this type of disease. Many dermatologists believe that in occupational dermatoses the disability can be reduced and in many cases prevented, and that under normal working conditions much can be done to lessen the toll that these skin disturbances take. Industry is interested in the prevention of such cases and the avoidance of complications, or at least in limiting the time lost to a short period of disability, with the desire to return workers early and to provide for the full production of the product involved. The employee, on his side, desires to maintain or even improve his earning power and is anxious to avoid lost time from illness. The medical profession is interested in working with both parties, detecting these cases early and providing treatment so that the period of disability will be little or none.

For the physician who sees many industrial cases — for example, the medical director of a large or small industrial medical department — there are certain measures that will aid him in preventing lost time and in reducing compensation paid and other expenses. He can find his cases early by training foremen and nurses to detect skin manifestations, and can send these workers to the plant dispensary for early therapy. If he is able to diagnose cases early or to obtain adequate consultation, a good beginning will have been made. If a cutaneous condition is found, it is necessary to exclude the

causative factors, if humanly possible, by obtaining aid in devising adequate preventive measures. Early treatment should be soothing, and care should be taken to avoid secondary infection. The selection of proper employees for hazardous jobs and a follow-up of those returning to work after a dermatitis will aid in preventing later recurrences and more disability.

* * *

In the larger aspects of losses due to occupational disability caused by cutaneous manifestations, there are several accomplishments to be attained. There should be further basic studies concerning the physiologic and chemical activities of the skin. Factories and working places should be provided with means and personnel for the early detection and treatment of occupational dermatoses. There should be available more statistics and more end-result studies of such occupational cases. There should be capable dermatologic representation on boards and commissions dealing with occupational dermatoses. There should be improved instruction in occupational dermatoses and in the dermatologic aspects of legal medicine pertaining to compensation cases. There should be adequate legislation in every state to cover all types of occupationally acquired dermatoses. Lastly, the medical profession must work with the law in the most effective and impartial analysis of claims and in the just disposition of cases.

416 Marlborough Street

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colonial author and published in London in 1647¹³ It reads as follows

Our young students in Physic may be trained up better than yet they bee, who have onely theoretical knowledge and are forced to fall to practice before ever they saw an anatomic made, or duly trained up in making experiments, for we never had but one anatomic in the country, which Mr Giles Firmin (now in England) did make and read upon very well, but no more of that now

The date and place of this dissection are not recorded Giles Firmin, a physician-clergyman, was in the Massachusetts Bay Colony from 1632 to 1646, at first resident in Boston but from 1638 to 1644 resident at Ipswich It is probable that the dissection was made at Ipswich One writer suggests that it was made on a body secured by robbing a grave Likelier it was on the body of an executed murderer, a procedure permissible under the common law and the code of 1641

The rarity of provision of the bodies of executed murderers for dissection in the early colonial period is indicated by a resolution adopted October 27, 1647, by the Governor and Council of the Massachusetts Bay Colony,¹⁴ reading as follows

We conceive it very necessary yt such as studies physick and chirurgery may have liberty to read & to anatomize once in four years some malefactor in case there be such as the Courte shall allow of

Records of human dissection in colonial New England are rare There were no medical colleges and no medical journals, and such events would not be likely to be published in any of the few newspapers of the eighteenth century because of the public aversion to the procedure

Dr William Hunter delivered lectures on anatomy at Newport, Rhode Island, in 1754, 1755 and 1756¹⁵ These were attended by both physicians and laymen His advertisements announcing the lectures made no mention of demonstrations of a dissected human cadaver Some writers have considered this omission as evidence that no demonstrations were given, but Dr Hunter would probably not have mentioned such an intention in an advertisement in a newspaper, even if he could have foreseen that some favoring judge would provide the body of an executed murderer

An earlier record is found outside New England Dr Peter Middleton and Dr John Bard made a human dissection in New York City in 1750^{16 17} The body was that of a murderer executed in New Jersey Dr Thomas Cadwalader, probably before 1751, and Dr William Shippen, beginning in 1762, gave lectures on anatomy in Philadelphia in which they demonstrated dissected human bodies¹⁸

These few records indicate the probable rarity of dissection of bodies legally acquired in the colonial period in New England The only legal source was the body of an executed murderer One writer^{19 20} says that the bodies of suicides were available for dissection in the colonial period A law adopted in the Massachusetts Bay Colony in 1660²¹ states

that a suicide is denied "the privilege of being buried in the common burying place of christians, but shall be buried in some common highway and a cart load of stones laid upon the grave as a brand of infamy" A search of the colonial laws reveals no provision for dissection of the body of a suicide, nor did the English common or statutory law carry such a provision, although the bodies of suicides were available at Edinburgh shortly before 1700 under an act of the local magistrates

Dr Harrington,²² writing about 1905, states that it was the rule in Massachusetts at the close of the Revolutionary War for the court to have discretion in allowing the dissection of the bodies of those executed for murder, arson or burglary I am unable to confirm this statement so far as it relates to the bodies of those executed for arson or burglary This statement is made in connection with several others that are apparently taken from an article published in 1896²³ Dr Harrington cites this article A careful reading of it brings the conclusion that he misinterpreted a somewhat obscure passage Neither the English common law nor statutory law, as already stated, provided that the bodies of those executed for arson or for burglary might be directed to be dissected, as were the bodies of murderers No provision for dissection of the bodies of those executed for arson or burglary occurs in the acts of the Legislature of Massachusetts in the colonial period nor in the early national period Such a statutory provision was made in New York in 1789 It therefore appears that the only legal provision for human dissection in the colonial period in New England came from an occasional additional sentence by a judge, in condemning a murderer, that his body should be dissected

An additional source was provided in Massachusetts in 1784 All the colonies enacted laws against dueling in the eighteenth century The law was revised in Massachusetts in 1784 when a statute entitled "An Act against Duelling" was passed²⁴ One of the provisions of this act provided that the body of one killed in a duel might either be buried without a coffin in a public place with a stake driven through the body — an ignominious form of burial — or be given to a surgeon for dissection In the case of one convicted of "murder in a duel" and executed, however, the body must be given to a surgeon for dissection If no surgeon applied for the body, the ignominious form of burial was to be used This statute is the first instance in New England of a law that was mandatory in regard to the giving of a dead body for dissection A statute was enacted in 1805 in Massachusetts²⁵ in which dueling was included with murder and some other crimes The mandatory feature regarding the body of a duelist was continued The specific law of 1784 regarding dueling was repealed in 1806, because the penalty for the crime was covered by the statute of 1805²⁶

In none of the laws of the several states of New England except that of Massachusetts was the feature of the dissection of the body of one engaged in a fatal duel included until the District of Maine became the State of Maine in 1820. Its first legislature adopted verbatim many of the laws of Massachusetts under which it had been governed as the District of Maine. One of these²⁷ provided for the dissection of the bodies of those who had engaged in a fatal duel. Fatal duels were few, so that these laws in Massachusetts and Maine provided little additional legal material for dissection.

The provisions for the dissection of the bodies of murderers and duelists were not specifically designed to advance the study of anatomy. They were in every case a further penalty for crime, and the availability of the body for dissection was only incidental to the main purpose of such provisions. Therefore these laws were not strictly anatomical laws, although they did incidentally provide legal material for the study of anatomy.

The first legislative act in the northeastern part of the United States that shows by its wording a purpose to provide for the study of practical anatomy was the direct result of a public disturbance. It became rumored in New York City in May, 1788, that a dissection was in progress on a body illegally disinterred. The public clamor resulted in a riot that became so serious that the state militia was called out to disperse the mob. This episode was known as "the doctor's mob."²⁸

The Legislature of New York at its next session enacted on January 6, 1789, a statute entitled "An Act to prevent the Odious Practice of digging up and removing for the Purpose of Dissection, dead Bodies interred in Cemeteries or Burial Places."²⁹ The first section provided penalties for the offense, the second is important enough to be quoted.

In order that Science may not in the Respect be injured by preventing the Dissection of proper Subjects, be it further enacted by the Authority aforesaid, that the Justices of the Supreme Court or of any Court of Oyer and Terminer and Gaol Delivery, in this State, from Time to Time, when any Offender shall be convicted before them or any of them of Murder, Arson, or Burglary for which he or she shall be sentenced to suffer Death, may at their discretion add to the Judgement that the Body of such Offender shall be delivered to a Surgeon for Dissection, and the Sheriff who is to cause such Sentence to be executed shall accordingly deliver the Body of such Offender, after Execution [is] done, to such Surgeon as such Court shall direct for the Purpose of aforesaid, Provided always that such Surgeon, or some other Person by him appointed for the Purpose, shall attend to receive and take away the dead body, at the Time of Execution of such Offender.

This law was not copied in any state in New England, but the fact that it put those executed for arson and burglary in the same class as murderers may have been an influence in laws later enacted in states of New England that extended the privilege of dissection to the bodies of other than murderers, especially in the law of 1824 in Connecticut, to be mentioned later.

The several states of New England, with the beginning of the national period, enacted codes of laws, but except in so far as these were contradictory to the English common and statutory law, under which these states had existed as colonies, the body of English law continued in force. James Kent³⁰ wrote in his commentaries on American law of the early national period as follows:

But though the great body of common law consists of a collection of principles, to be found in the opinions of the sages or deduced from universal usage and receiving progressively the sanction of the courts, it is nevertheless true that the common law, as far as it is applicable to our situation and government, has been recognized and adopted, as one entire system in the constitutions of Massachusetts, New York, New Jersey and Maryland. It has been assumed by the courts of justice, or declared by statute, with like modifications, as the law of the land in every state.

Therefore the availability of the bodies of executed murderers for dissection at the discretion of the sentencing judge continued to be a source of material for anatomical study. In some states the procedure was expressly stated in the statutes, in others it was followed only under the ancient common law. In one state of New England this procedure is contained in the anatomical law now current.

Thus the availability for dissection of the bodies of those executed for murder, and after 1784, of those engaged in duels in Massachusetts, was the only legal source of material for dissection in any state in New England during more than two hundred years after the first settlement in 1620. Few bodies were available from this source. A statistical compilation made in Massachusetts in 1830 showed that for the thirty years from 1800 to 1829, inclusive, the total number of executions in that state averaged only little over two a year, and by no means all those to be executed were further sentenced to be dissected.

Inasmuch as this provision was only incidental to the punishment of arch criminals, in the public mind dissection was placed in close relation to major crime and brought the conviction that dissection was an ignominy, and that anyone whose body was dissected suffered posthumous disgrace and was thereby allocated to the same class as murderers, a belief that accentuated the aversion to dissection arising from sentiment.

The number of medical colleges increased until in 1823 there were eight of them in New England. There was a corresponding increase in the number of medical students. All students were expected to do human dissection, although no such requirement was printed in the announcements or catalogues of the colleges. The provision for legal acquisition of bodies for dissection was no broader than in 1784, forty years earlier, when there was only one medical college in New England. The only method of adequate provision for human dissection was increasing recourse to grave robbing. The alternative was the abandonment of the teaching of practical anatomy.

Elsewhere I²¹ have discussed the extent of grave robbing in New England.

A slight relief came in Connecticut in 1824 with the enactment of a law providing that all bodies of those who died in the State Prison or who were executed for any crime, unless claimed by kindred, should be delivered for use in the teaching of anatomy.²² Previously the state had maintained a cemetery at the State Prison in which were buried the unclaimed bodies of those who died or were executed in that institution. This was the first law in New England to provide for the anatomical study of bodies other than those of murderers and duelists.

The Second Phase

The extension of legal sources of material for human dissection in the states of New England was the indirect result of a series of events in another country, events familiar to all those interested in medical history. The immediate cause of these events is less well known.

Edinburgh was a center of medical education in the early nineteenth century. Anatomy had been taught in institutions in that city for more than a hundred years—since early in the eighteenth century. The methods of visual instruction, however, were restricted to charts and demonstrations of prosected cadavers in amphitheaters. Only a few favored assistants of the professors had the privilege of personally engaging in dissection. The great majority of medical students never applied a scalpel to a dead human body and got no nearer to a cadaver than a seat in an amphitheater during a demonstration. These methods of teaching required only a few cadavers, those bodies of prisoners dying in the House of Correction.

A change came in 1826 when the College of Surgeons of Edinburgh announced that thereafter every medical student who desired the degree of Doctor of Medicine must personally engage in dissection. The University of Edinburgh made a similar requirement a year later.²³ This greatly increased the demand for dead bodies. The prices paid for them advanced, causing increasing activity of the resurrectionists that led to publicity and to public clamor in Scotland and England regarding grave robbing. The British newspapers published much on the subject, and a considerable part of this material was reprinted in American newspapers. The knowledge of events in Great Britain reached legislators as well as all members of the American public, and it seemed to the medical profession a favorable time to secure legislative reform of the inadequate legal provisions for the study of practical anatomy.

The public became conscious that grave robbing was more frequent than had been suspected, and the prejudices against dissection and medical colleges were accentuated. The medical profession had long desired legal provision of

teaching practical anatomy, for grave robbing was distasteful to all its members. Individual physicians and small groups of them had repeatedly asked legislatures to provide relief. This was usually spoken of as "legalizing anatomy," a somewhat misleading phrase, because anatomy was never illegal in New England, nor was dissection. The illegality pertained only to some methods of procuring dead bodies.

Legislators had given little heed to these requests of physicians because of the well-known popular aversion to dissection. Occasionally a bill was introduced in a legislature by a physician who was a member of the body. Such bills rarely got beyond reference to a committee that declined to report the bill for a vote.

The first concerted action in New England began in the Massachusetts Medical Society on February 4, 1829, when Dr. Abel Lawrence Peirson introduced a resolution to appoint a committee of the society to seek legislation.²⁴ He was appointed chairman of a committee and continued as chairman of an enlarged committee appointed a few months later. He gave much time and effective effort to the work. A survey of the activities of the next few years leads to the conclusion that Dr. Peirson more than any other one man deserves the credit of securing the legislation that followed. This conclusion is not in accord with that of another writer,²⁵ who in 1896 stated that Dr. John C. Warren, professor of anatomy in the Harvard Medical School, was largely responsible for the legislation. This writer was a grandson of Dr. Warren.

A long, argumentative circular letter was sent to each member of the medical society asking him to try to influence such members of the Legislature as he knew personally.²⁶ This letter was dated September 1, 1829, at Salem, where Dr. Peirson was in practice, and was probably written by him. A bill was introduced in the session of the Legislature of January, 1830. It was referred to a committee, which reported that it "did not think it expedient to propose any alteration of the laws at the present time, because in a community like ours, it is necessary that laws should proceed from and be supported by public opinion."²⁷

The committee of the Medical Society sought to educate the public, and articles signed by members of the committee were published in newspapers. A pamphlet was prepared arguing the desirability of the proposed law, and 10,000 copies were ordered printed for distribution throughout the state.²⁸

The bill was again introduced at the session of May, 1830. The Governor, in his address at the opening of the Legislature, discussed the desirability of better provision for teaching anatomy.²⁹ This part of his address was referred to a special committee. The bill was postponed to the next session.

An argument publicly advanced was that adequate legal provision for human dissection

benefit the poor, because if all medical students could have instruction in practical anatomy all physicians could acquire this knowledge instead of its being largely restricted to those who could go to Paris, where material for dissection was abundant, and who on returning charged larger fees and were usually employed only by the well-to-do.⁴⁰

On invitation Dr John C Warren addressed a joint session of the Legislature on February 2, 1831, on the subject.⁴¹ He was a member of the committee of the Massachusetts Medical Society and professor of anatomy and surgery in the Harvard Medical School, and was well and favorably known throughout the state. The bill was passed in the session of January, 1831, under the title, "An Act more effectively to Protect the Sepulchres of the Dead and to Legalize the Study of Anatomy in Certain Cases."⁴² This is considered the first effective anatomical law in any English-speaking country. It antedated the Anatomy Act of the English Parliament by fifteen months.⁴³

The new Massachusetts law permitted civil officials to surrender for dissection any body that must otherwise be buried at public expense, with some exceptions, thus going far beyond the former limitation to the bodies of major criminals. Preference in delivery of such bodies to physicians was to be given to those who were teachers in a legally chartered medical college in the state. Harvard Medical School and the Berkshire Medical Institution were the two chartered medical colleges in Massachusetts at that time. The law received public approval.⁴⁴

This legislation was defective in two major respects, the first being that it was not mandatory, but only granted permission to civil officials to deliver bodies for dissection at their discretion, and the second being that it included several exceptions that tended to nullify its purpose. Officials were not permitted to deliver for dissection the body of any stranger, any town pauper, any person who during life had requested that his body be buried or any person whatsoever if within thirty-six hours a kinsman or friend requested that the body be buried.

The earlier sections of the law provided penalties for disturbing graves or disinterring bodies and by specific statement repealed former laws on this subject. This repeal was one of the most important features of the new law, because the law of 1815, in Massachusetts, had provided the same penalties for possession of a disinterred body as for the disinterment itself.⁴⁵ Possession was defined as presence of a body on premises controlled by the accused, and the penalties were heavy fines and imprisonment. The matter of possession was not mentioned in the law of 1831. Although the primary stimulus of the activities that secured this law was a series of events in Scotland and the publicity given to them, here expressed the opinion that local

events in Massachusetts a few years earlier had a large influence, especially in securing the effective interest of Dr Peirson.

The law was somewhat improved by amendments in 1834.⁴⁷ During the next forty years the law was amended several times without extensive modification of its provisions. The amendments concerned additions to the list of public institutions from which bodies might be delivered and changes in the titles of governing authorities of these institutions.

The enactment of this law in Massachusetts had an effect in neighboring states. Connecticut passed a law in 1833 providing that all bodies to be buried at public expense were to be available for dissection,⁴⁸ but this was repealed exactly a year later.⁴⁹

An anatomical law was passed in New Hampshire in 1834 that was a close copy of that of Massachusetts,⁵⁰ but this was repealed in 1842 after having been in force for only eight years.⁵¹ A group of physicians in Vermont in 1835 tried unsuccessfully to secure passage of a law similar to those of Massachusetts and New Hampshire. I have found no record of attempts at this time to pass similar laws in Maine or Rhode Island.

To summarize the events of the second phase, an anatomical law was passed in Massachusetts in 1831 and was continued on the statute books. A law of this nature was passed in Connecticut in 1833 and was repealed after one year, although the law of 1824 in that state regarding the bodies of those who died or were executed in the State Prison continued in force. A law passed in New Hampshire in 1834 was repealed after eight years. No similar law was enacted in Maine, Rhode Island or Vermont.

The fact that Massachusetts secured and maintained an anatomical law, whereas in Connecticut and New Hampshire such laws were passed but soon repealed and in the three other states of New England no such laws were secured, suggests some influences in Massachusetts not found in the other states. Two may be conjectured, the first being that the extensive program of education of the public concerning the desirability of an anatomical law in Massachusetts made by the Massachusetts Medical Society in 1830 had a continuing effect. The other is that many members of the Legislature in Massachusetts were graduates of Harvard University, which may have had some influence on these legislators regarding a law that much concerned the medical school of that university. New York was the only other state in which an anatomical law enacted before 1860 continued in force.

The Third Phase

The influences that brought about a third phase of anatomical laws in New England were not local to that area. The organization of the American Medical Association in 1847 had two major objects. One of these was the improvement of medical educa-

tion In that society and in many state medical societies papers were read, committees appointed and resolutions adopted, all of which had no marked immediate result In a few colleges the length of the medical session was slightly increased, but the leading deficiencies of lack of standards in preceptorial teaching and the repetitive curriculum were not eliminated, and the medical-education program of 1860 was not materially better than that of 1830

Some concerted demonstration of educational weakness was needed to bring reform The first establishment of medical colleges in the American colonies was the result of evidence of medical deficiencies in the French and Indian War

Similarly, it was the Civil War that influenced improvement needed in that era Medicine and surgery had shown many deficiencies in the field After the close of the war a definite and concerted action began to improve the program of medical education A convention of medical teachers held in 1867 advocated lengthening of the teaching session, increase of the number of sessions to be attended before receiving the degree of Doctor of Medicine and a graded curriculum Emphasis was placed on needed improvement in certain subjects Two of these were practical anatomy and operative surgery on the cadaver Such extensions would require the availability of more cadavers

These conditions were probably responsible for introducing the events of the third phase of anatomical laws, which was the extension to other states in New England of laws similar to the one that had been in force during more than thirty-five years in Massachusetts

The first legislative response in New England occurred in March, 1869, with the passing of a law in Maine permitting bodies that must otherwise be buried at public expense to be surrendered for dissection⁵² A similar law was passed three months later in New Hampshire, which closely resembled the law that had been in force in that state from 1834 to 1842⁵³ Connecticut delayed until 1871⁵⁴ Vermont did not join these three states in passing a permissive law at this time Rhode Island has had no medical college since 1828 and has never had an anatomical law

The anatomical laws passed in Maine, New Hampshire and Connecticut from 1869 to 1871, together with the law of Massachusetts passed in 1831, had certain basic similarities, but some of them had provisions not found in other states The common provisions were three first, that a body delivered for dissection should be used only for the advance of anatomical and surgical science, second, that the body should not be transported beyond the boundaries of the state in which it was surrendered, and third, that after the body had been used for dissection the remains should be given decent burial

The Maine law had a peculiar provision as its first section, which was that if a person requested or consented before death that his body be used to advance anatomical science, it might be so used if no kindred objected This is in direct conflict with the legal principle in force for many centuries that a person cannot devise by will or by contract or otherwise direct what disposal shall be made of what will later be his dead body, because a dead body is not property This principle has been upheld by many court decisions both in Great Britain and in the United States, some of the decisions being in state supreme courts in the twentieth century

The two major deficiencies already mentioned regarding the Massachusetts law of 1831 were continued in these laws of the third phase, namely, that the laws were only permissive and not mandatory regarding the acts of civil officials, and that exceptions were made in regard to strangers, those who requested before death that they be buried and those for whom burial was requested by a kinsman or friend This last exception was the most troublesome one A friend might be an undertaker who wanted to be employed to conduct a funeral, or even a laborer who desired the job of digging a grave These conditions were later remedied in some states by amendments that restricted kinsmen to spouses or those related by blood, and friends to those who had been legal representatives of persons before their death The exception of strangers was also later limited by excluding from the group any person known as a vagabond or tramp

The major weakness of the anatomical laws of the third phase was that they provided for discretionary action instead of mandatory action for civil officials in control of dead bodies that must be buried at public expense Some of these officials had a personal aversion to dissection Others disliked to make a decision that sent a body to the dissecting table because it brought criticism from those who had known the dead person in life In some cases a decision to order a body for anatomical study was used to oppose the official rendering the decision for further elective office

Opinions were expressed, and sometimes definite charges were made, that officials accepted or even solicited bribes for surrendering a dead body This is the source of the provision in many modern anatomical laws for penalties against any official who accepts recompense for delivering a dead body for dissection, heavy fines, or in a few laws imprisonment, being prescribed

A further difficulty was that from time to time an official favorable to surrendering bodies for dissection was replaced by one who was unfavorable, so that any institution might suddenly find a main source of supply of cadavers eliminated All these conditions, and some others, made the supply of

cadavers from legal sources uncertain, sometimes extremely so, and at others more expensive than grave robbing, which therefore continued to supplement the uncertain and inadequate supply from legal sources

The enactment of new anatomical laws in the sixties and seventies was not confined to New England. Similar laws appeared in states farther west, most of them a little later. Fourteen states had such laws before 1880. In all these the permissive feature predominated, although some of them had mandatory provisions regarding small categories, mainly the unclaimed bodies of those who died in state prisons.

The Fourth Phase

The fourth phase of the anatomical laws of New England began in the eighties. The conditions under the permissive type of law convinced all those engaged in the teaching of anatomy that the laws should be amended to substitute for the discretionary action mandatory directions to govern the actions of civil officials and employees in the surrender of dead bodies under their control.

Many factors entered the problem, a few will be mentioned. The relative influence of each of these varied in different states. Nearly all medical practitioners, remembering their own difficulties as students, were favorable to the change. Some of them were personal physicians of legislators and were able to influence them. A state medical society by resolutions and through a committee could influence the legislature of its own state as a body.

Between 1875 and 1890 the medical-education program changed greatly. The teaching session was lengthened. The requirement of attendance to be eligible for the degree of Doctor of Medicine was increased from two to three sessions. The graded curriculum was introduced, and along with it laboratory teaching in several subjects. This brought a different type of teaching in practical anatomy. The old method of hasty dissection of unembalmed bodies disappeared. Embalming was introduced and methods of storage of cadavers were much improved. This permitted acceptance of bodies from legal sources and their accumulation during the months that a medical college was not in session, and the former practice of completing a dissection in a week gave way to the spending of several weeks in the procedure, with much more attention to anatomic details. All medical colleges and their teachers favored a method that would give a more certain supply of cadavers and permit abandonment of the distasteful, illegal and uncertain reliance on grave robbing. Medical colleges as institutions and universities engaged in medical education were influential in inducing legislatures to institute reform.

Aside from the medical profession, medical teachers and medical teaching institutions, two other

influences deserve mention. The majority of civil officials and employees disliked the duty under the permissive laws of deciding in each case whether to send a dead body to the dissecting table or to bury it at public expense. Whatever they did brought criticism, although from different sources. Mandatory laws would relieve them both of decisions and criticisms.

The aversion of the public to dissection had abated since earlier in the nineteenth century, when each detected case of grave robbing received publicity in the newspapers, which aroused public sentiment. The newspapers said little or nothing about the few detected episodes, and the great majority of grave robberies were not discovered because the technic of the procedure had become a fine art and the emptying of a grave seldom became known to the general public. Also, because the permissive laws made the surrender of dead bodies for dissection legal, the public came to believe that all bodies used for dissection were secured legally, a misconception nurtured by the medical profession.

These and other factors brought the support of legislators to amendments to the anatomical laws. After such amendment had been accomplished in one state it became easier to secure a mandatory law in a neighboring state.

Although Vermont did not join the four other states in New England that had medical colleges in enacting a permissive law about 1870, she led in passing an entirely mandatory law in November, 1884.⁵⁵ It directed that overseers of the poor in any town and superintendents of state institutions must, on written request of any licensed physician or surgeon resident in the state, surrender for the advancement of anatomical science any body that must otherwise be buried at public expense. The bodies of certain persons were excepted.⁵⁵ It was nine years before the next state in New England followed. Connecticut in 1893 enacted a similar mandatory law.⁵⁶ Then came corresponding laws in New Hampshire in February, 1897⁵⁷, in Maine in March, 1897⁵⁸, and in Massachusetts in 1898.⁵⁹ Rhode Island, never having had an anatomical law, did not enter into the fourth phase, just as she had not participated in the second and third phases. The enactment of these mandatory laws terminated the procedure of local grave robbing and the traffic in dead human bodies by importation from more distant states. These would have ceased long before if legislators had sooner followed the desires and advice of the medical profession.

PROVISIONS OF CURRENT ANATOMICAL LAWS IN NEW ENGLAND

Few amendments have been made to the anatomical laws of New England in the twentieth century. The discussion that follows is based on examination of the latest editions of the revised

statutes of Connecticut,⁶⁰ Maine,⁶¹ Massachusetts,⁶² New Hampshire⁶³ and Vermont⁶⁴ The laws of each of these states for each year since the issue of the latest edition of its revised statutes have been examined for possible amendments The use of the word "all" in what follows pertains to these five states only Rhode Island, having no anatomical law, does not enter the discussion until the last paragraph of the section is reached The keystone of all current anatomical laws is that the dead body concerned must be buried at public expense if it is not used for anatomic study Certain exceptions will be mentioned later.

Members of a group of named civil officials and employees of political divisions have the duty to notify certain specified legal recipients when a body that must be buried at public expense comes under their control, and when the recipient has made a written request for the body they have the further duty of delivering it to him Penalties are provided for failure in these duties If no request is received, the body must be buried at public expense

Kindred by blood or marriage, and in some states others, such as officers of fraternal organizations, may request that such bodies be buried at the expense of the claimant, and if such petitions are made within a specified time, varying in different states, they have priority over requests for the body to be used for dissection

Three requirements are imposed on the recipient in all states The body must be used only for advancement of anatomical, medical or surgical science or for medical education, its use must be confined to the state in which it is surrendered to the recipient, and after such use the remains must be decently buried The recipient must give a bond that these requirements will be observed, in all states except Vermont, where a penalty is provided for non-observance

The phrase "decently buried" as applied to the remains of a dissected cadaver goes back at least to the charter granted to the College of Physicians of London by Charles II in 1663 None of the anatomical laws in New England define decent burial, as regards what is to be buried and where and when No definition is given regarding what constitutes "remains," and whether these include only the skeleton or parts of it or the detached soft parts No time of burial is specified Some hold that this omission makes it legal to keep the remains or parts of them for an indefinite period of time before burial An early law in one state specified that the burial must be made in a public cemetery, but this is omitted in later revisions There is no provision that the remains of each cadaver shall be buried in a single excavation

The law of Connecticut says that burial must accord with the rules of the State Board of Health A specification in another relation in this statute uses the words "buried or cremated" which sug-

gests that cremation is considered equivalent to burial, but there is no suggestion concerning whether the cremation must be in a licensed public crematory Possibly court decisions or rulings of boards of health have defined decent burial, but so far as the anatomical laws go, the requirements are hazy

The legal recipient of dead bodies destined for dissection varies in the different states In Vermont, the recipient is any licensed physician resident in the state In New Hampshire, the recipient is any licensed physician in the state, with preference given to such as are instructors in a medical school legally established within its borders In Massachusetts, the recipient is the dean or other officer of any medical school legally established in the state Connecticut is the only state in which the recipient is not a person or persons, there it is the Medical Department of Yale University In Maine, the original recipient is any member of an anatomical board or the board as a whole This board has the duty of distributing the bodies received to medical colleges or to persons who become the final recipients and use the body This board was created by the law of 1897, and is the only one of its kind in New England Originally the members were specified as those holding certain teaching positions in medical colleges in the state The only medical college in the state was suspended in 1921 Ten years later the law was amended so that the superintendents of four named hospitals should constitute the membership of the board The law in Maine is entitled "to provide for medical education", in the amendment of 1931 premedical education and nursing education were specifically construed to be a part of medical education, and four colleges of arts in the state were named as legal recipients of dead bodies to conduct medical education under this construction⁶⁵

In only Maine and Connecticut does the anatomical law require any record of bodies received for dissection In Maine, the record is made by the Anatomical Board, without specification as to what shall compose the record In Connecticut, the recipient must make a record of the sex and, if known, the name and last place of residence No descriptive record of stature, marks of identification or other details is suggested

The exceptions to requirements of delivery for dissection of bodies that must otherwise be buried at public expense go back to early laws In all states the body of a traveler or stranger who dies suddenly must be buried rather than be surrendered for dissection Tramps, vagabonds and vagrants are excluded from this rule in Connecticut, Maine and New Hampshire The anatomical laws of Massachusetts, New Hampshire and Vermont provide that the bodies of soldiers and sailors and of members of the Marine Corps who have served in any war of the United States and have been honorably discharged must be buried rather than delivered for dissection In one state, however,

of these men are included. No mention of these restrictions is made in the law of either Connecticut or Maine, but in the former a law in another connection provides that men of these groups shall be buried at public expense.

The ancient provision still prevails in the anatomical laws of Connecticut, Massachusetts and Vermont that if a person requests in his last sickness that his body be buried, this must be done at public expense rather than have the body delivered for dissection. It has already been stated that the provision that a body must be buried at public expense if a kinsman so requested was a serious deterrent to the teaching of anatomy in the nineteenth century. This provision is still found in the law in Vermont.

Provision for the payment by the recipient of expenses connected with the transportation and burial of a cadaver is found in the anatomical laws of Vermont and Maine, but is not mentioned in those of other New England states.

Peculiar provisions are found in the laws of some of the states. The anatomical law of Connecticut states that the bodies of those dying from certain named contagious diseases shall not be available for dissection. The first disease named is Asiatic cholera, indicating the ancient origin of this section. A former law included those dying from unknown diseases because they might be contagious. It seems that such provisions belong in laws relating to the boards of health rather than in anatomical laws. The law also provides that the head of every educational institution that teaches anatomy must give a bond that no bodies illegally secured will be allowed to come within the premises under his direction. This law goes back more than a hundred years to the time when grave robbing was prevalent.

The provision regarding receiving the body of one who before death requested or consented to dissection of his body, which has already been mentioned as the first section of the law of 1869 in Maine, is still a part of the statute in that state. A physician who taught anatomy many years in Maine informs me that he knows of only one body that was received under this provision over a long period.

The most ancient relic in current anatomical laws in New England is in Massachusetts, where a judge may still order the body of an executed murderer to be dissected. This goes back to English common law before 1540.

All six of the states of New England still have laws against illegal disinterment of the dead, commonly called grave robbing, and impose penalties of fines or imprisonment or both. The fines extend to a maximum of \$3000 in one state, and the maximum period of imprisonment to fifteen years in one state.

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The history of the development of laws for the legal acquisition of dead human bodies for dissection in New England covers the more than three

hundred years since its first settlement in 1620 and goes back at least another hundred years in the English common law. This history in the last one hundred and fifty years has included many endeavors and many disappointments on the part of the medical profession of New England.

The changes in this area were few until 1830. Four periods are found in the extension of legal provisions in New England: the first from 1641 to 1824, the second from 1831 to 1842, the third from 1869 to 1871 and the fourth from 1884 to 1898.

The few amendments made to the anatomical laws since 1898 indicate that teachers of anatomy in New England have felt reasonably secure in the legal acquisition of enough cadavers to meet their needs. The supply has varied with public economic conditions. One cannot predict future conditions, but recent diminution in the supply of cadavers is already causing anatomists to ponder on what the future will bring with increasing public provision for all classes of people, especially that class from which cadavers have usually been drawn.

The variations noted in the anatomical laws of the closely associated states of New England suggest that the anatomists should endeavor to formulate an anatomical law that includes the favorable parts of current laws and removes the unfavorable and redundant provisions. Such a formulation may become useful when opportunity is presented to amend and revise these laws, not only in New England but in every state of the Union.

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INFECTIOUS MONONUCLEOSIS*

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INFECTIOUS mononucleosis, or glandular fever, was first described in 1889 by Pfeiffer¹. The earliest report on the subject in this country was that by West² in 1896. The hematologic aspects of the process were extensively studied during the first three decades of this century and were crystallized by the work of Downey and McKinlay³ in 1923. In 1932, Paul and Bunnell⁴ observed that the serum of patients with infectious mononucleosis agglutinated the erythrocytes of sheep in concentrations above a normal titer. Since then there have been numerous reports on the disease, outstanding of which is the classic review by Bernstein⁵. In that monograph, the literature is reviewed and the vagaries of the disease are discussed in some detail. Numerous investigations have been made regarding the etiology of infectious mononucleosis, but no definite causal factor has yet been found.

Contratto,⁶ of the Stillman Infirmary, Harvard University, has reported the largest single series to date, dealing with subject matter similar to that discussed in this paper.

The material for this report came from two sources: Dick Hall's House, the infirmary of Dartmouth College, and the Mary Hitchcock Memorial Hospital. The cases are those seen from January, 1935, to January, 1945. Both institutions are staffed by the same men, and all studies are done by the same laboratory. It was believed that a comparison of the two groups of cases, seen by the same physicians, would be of interest.

INCIDENCE

Of the 141 cases in both institutions with a final diagnosis of infectious mononucleosis, 111 (82 in Dick's House and 29 in the hospital) were acceptable for study. The remaining 30 were discarded for various reasons, including inadequate records, insufficient data for diagnosis and missing laboratory studies.

The 82 infirmary cases represent 0.74 per cent of the total admissions for the period covered, and the 29 hospital cases represent 0.07 per cent. This difference is not surprising if one recognizes the specific age group that Dick's House serves. All the patients there were college students, save one who was a house officer of the hospital. In the hospital cases, it was interesting to note that 8 patients were from its nursing staff.

The yearly incidence shown in Table 1 roughly follows the number of general admissions for the year. The disease never occurred in epidemic proportions, although several such instances have been reported. Nor has the disease been seen in roommates, in spite of the fact that many of the

TABLE 1 Number of Cases according to Years

YEAR	DICK'S HOUSE	HOSPITAL	TOTALS
1935	3	0	3
1936	5	2	7
1937	2	3	5
1938	8	1	9
1939	15	3	18
1940	14	6	20
1941	9	5	14
1942	11	3	14
1943	9	3	12
1944	6	3	9
Totals	82	29	111

patients were sick for several days before admission.

Some observers believe that there is a seasonal incidence of this disease. This has not been clearly borne out in the present series, as evidenced by Table 2, which shows the incidence by months. The reason for the relative paucity of cases during the summer months is that until 1942 the college infirmary was closed from the latter part of June until the first part of September. The relatively high summer incidence in the hospital, on the other

TABLE 2 Number of Cases according to Months (1935-1944)

	DICK'S HOUSE	HOSPITAL	TOTALS
January	12	2	14
February	8	2	10
March	8	0	8
April	8	1	9
May	10	2	12
June	7	6	13
July	1	6	7
August	3	3	6
September	6	2	8
October	5	2	7
November	5	2	7
December	9	1	10
Totals	82	29	111

hand, is probably due to the influx of campers into the surrounding territory. Four of the hospital cases were in this category.

Infectious mononucleosis is a disease of the younger age groups. Cases occurring in the sixties and even one at the age of seventy have been reported. In the Dick's House series, the average age was 20.2 years, with the youngest patient seventeen years old and the oldest thirty-one. In the hospital there was a greater spread in the age incidence, the youngest patient being ten years old and

*Presented at the annual meeting of the New Hampshire Medical Society, Manchester, May 15, 1945.

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the oldest forty-six, with 5 patients over thirty. The average age, 22.6 years, was slightly higher than that in the infirmary group.

The sex distribution was naturally irregular. All the Dick's House patients were men, whereas in the hospital group there were 18 females and 11 males. Previous general studies have shown a slight preponderance of males.

CLINICAL MANIFESTATIONS

The protean nature of infectious mononucleosis has already been mentioned, and a review of the symptomatology confirms this. In Table 3 the complaints, both major and secondary, noted on admission in the combined series are listed. This table shows the most frequent symptoms, which are nonspecific. Sore throat was by far the outstanding single complaint and was evident in 65 cases on admission. During the course of their illness several more patients developed this symptom, so that by discharge 83 patients had complained of it at some time. The degree of soreness

TABLE 3 Major Symptoms in Both Series of Cases

SYMPTOM	No. of CASES
Sore throat	65
Grippal symptoms	52
Headache	35
Fatigue	16
Lymphadenopathy	15
Fever	13
Chills	11

varied from mild dryness or scratchiness to severe pain with inability to swallow. It is worthy of note that in a number of cases the sore throat at the onset was unilateral. Many of these patients developed a typical Vincent's type of ulcer.

The grippal symptoms included malaise, aches in the arms and legs, backache and neck ache.

Headache was the next most striking single symptom, it was frequently the only complaint. It varied from severe to quite mild, and was usually generalized or frontal. In no case was meningitis suspected, and no lumbar punctures were done.

In most cases the presenting symptom of fatigue had been present for some time. One student entered with this as his only complaint. He had become aware of it by observing his progressively decreasing ability to keep up with his mates on the swimming team.

Feverishness and chills occurred and the chills were often true rigors, especially in cases with marked throat involvement.

The rest of the complaints have been grouped by systems (Table 4). Under gastrointestinal symptoms are included nausea, vomiting, diarrhea and abdominal pain. The last-named was usually associated with diarrhea or vomiting, but in 4 cases it was in the left upper quadrant and was undoubtedly

ly related to splenic change. In 1 case the spleen had ruptured.

The respiratory symptoms ranged from a mild cold to a severe cough with manifestations suggestive of pneumonia.

The neuromuscular symptoms were comparatively unrelated, consisting of dizziness, nervous-

TABLE 4 Symptoms by Systems in Both Series of Cases

SYSTEM	No. of CASES
Gastrointestinal	28
Respiratory	19
Neuromuscular	8
Cutaneous	4
Ocular	5
Cardiovascular	2
General	6

ness, drowsiness, mental confusion—in a patient who became frankly delirious—and pain in the arm.

The skin changes consisted of boils or a rash.

The eye symptoms were unusual. Three patients presented watery eyes as the only early complaint, and 2 others noted marked puffiness of the lids.

Two patients entered with tachycardia as the only symptom.

The general symptoms were confined to 4 patients who complained of weight loss and 2 who on admission had no complaints referable to the disease and were hospitalized because of skiing injuries. In the latter cases, lymphadenopathy was discovered on the admission physical examination and the disease was diagnosed after blood-cell counts and agglutination tests had been reported.

PHYSICAL SIGNS

The throats of only 25 patients in both groups were considered normal on admission. The remainder showed varying degrees of inflammation. Thirty-two exhibited exudate on the lymphatic tissue of the tonsils or pharynx. Six showed frank ulceration of the fauces or tongue. One patient had a full-blown peritonsillar abscess, and another developed a lingual abscess later in the disease. Petechial areas on the soft palate, quoted by several authors as a fairly frequent finding, were present in 3 cases.

Smears and cultures were done in 49 cases. A beta-hemolytic streptococcus was isolated in 7 of these, Vincent's organisms were observed in 22, and a mixed infection was present in 20.

Marked gingival involvement was seen in only 2 cases, being accompanied in both by a pharyngeal infection of the Vincent's variety. Because of the frequent association of Vincent's infections and infectious mononucleosis, any case in which the diagnosis of Vincent's tonsillitis or gingivitis is made should be watched closely, with repeated studies, to exclude a possible underlying infectious mononucleosis.

Fever was absent in only 3 cases in both groups. The average temperature on admission was 100.6°F in the hospital group and 100.4°F in the infirmary group. The highest temperature recorded was 105°F in Dick's House (2 cases) and 104°F in the hospital.

The mean duration of fever was 5.9 days in the hospital group and 7.2 days in the infirmary group. In the latter, 2 patients were febrile for twenty days and 1 for nineteen days, whereas the longest duration of fever in the hospital was fifteen days. The fever follows no orthodox pattern and may return after an early subsidence usually with the onset of some complication.

The lymph-node enlargement that is characteristic of this disease and gives it the name "glandular fever" was pronounced in some cases and minimal or absent in others. Table 5 shows the extent and

TABLE 5 *Lymphadenopathy*

LOCATION	DEGREE OF ENLARGEMENT*			TOTAL NUMBER OF CASES
	SLIGHT	MODERATE	MARKED	
Anterior cervical	5	72	13	90
Posterior cervical	2	42	6	50
Axillary	0	32	3	35
Inguinal	0	28	2	30
Epitrochlear	0	11	1	12
Preauricular	0	1	0	1

*"Slight enlargement" signifies nodes slightly under 1.0 cm in diameter, "moderate," up to 1.5 cm and "marked" 2.0 cm or greater.

degree of involvement in the two groups. As a rule, the nodes are firm, discrete and either non-tender or very slightly tender. Occasionally with severe throat infections the tonsillar nodes are exquisitely tender.

In 9 cases, — 3 in the hospital and 6 in the infirmary, — there was no demonstrable lymphadenopathy, but in 3 of these there was a definitely palpable spleen. Ten cases showed lymphadenopathy elsewhere than in the anterior cervical chain, which was involved alone in 35 cases. In 2 cases in each group, there was isolated enlargement of the posterior cervical chain. In no case was isolated axillary, inguinal or epitrochlear enlargement found, nor was there any positive evidence of mediastinal or mesenteric lymphadenopathy.

The incidence of splenomegaly in infectious mononucleosis varies greatly in the published reports, with an average of 50 per cent of all cases showing this important sign. Press, Shlevin and Rosen⁷ report the incidence in a recent series as 72 per cent. There was a palpable spleen in 15 cases (53 per cent) in the hospital group and in 33 cases (40 per cent) in the infirmary group. It is of interest that the percentage was considerably higher in the last half of the study, from 1940 through 1944 — 58 per cent and 59 per cent, respectively. This probably represents no change in the disease but rather gives evidence of a more careful search on the part of the staff and the house officers.

The spleen in most cases was firm and nontender and was felt with difficulty, although several cases

demonstrated enlargement 4.0 cm below the left costal margin. In 4 cases, there was distinct tenderness in the splenic area.

Jaundice occurred in 3 cases, — 2 in the infirmary and 1 in the hospital, — but in 1 of the former there had been pre-existing chronic biliary infection. In the other cases the jaundice was moderate, with icteric indices of 24 and 29, respectively. Six other cases were reported as appearing jaundiced, but the icteric index was normal.

Associated with the sallow, waxy color that was mistaken for jaundice there was a mild facial edema, occurring for the most part about the eyes. This was present in 5 of the students and in 1 of the hospital cases. In 2 cases the appearance was striking enough to suggest the diagnosis of acute nephritis or trichinosis.

Cutaneous changes were evident in 9 cases. In the hospital group (2 cases), an extremely ill patient developed a generalized maculopapular eruption that rapidly became hemorrhagic. The other patient showed multiple ecchymoses, unassociated with thrombocytopenia or some other blood anomaly. These cleared spontaneously. Five of the infirmary patients showed a faint erythematous rash on the trunk and arms, which lasted for only a day. The others had a generalized maculopapular eruption for two days and were at first thought to have rubella.

Neurologic manifestations other than headache were infrequent. None were present in the hospital group, and in the infirmary they were seen in only 2 patients. One of them was the patient previously mentioned who became delirious at the height of the fever. The other entered with the complaint of "neuritis" in the left arm, which was actually a pain in the ulnar aspect of the forearm. The only finding was that of several large lymph nodes in the left axilla. These promptly disappeared, and with them the discomfort.

BLOOD FINDINGS

Examination of a stained blood smear is the simplest method of establishing the diagnosis in a suspected case of infectious mononucleosis. The characteristic picture shows a moderate leukocytosis, with a mononuclear percentage above 60. The mononuclear cells consist of normal monocytes, normal lymphocytes and the so-called "toxic lymphocyte," which is typical of the disease. The last-named cell makes up the majority of the mononuclear elements. It has certain distinct characteristics. It is variable in size, shape and staining properties. The nucleus, whatever its shape, is usually stained darkly and coarsely. The cytoplasm may be pale blue but is oftener deeply basophilic and vacuolated, presenting a foamy appearance. Since there was no significant variation in the blood picture in the two groups, they will be discussed together.

The average white-cell count on admission was 10,600, only a slight increase over normal. The highest admission count and also the highest count throughout the illness was 33,600. Not infrequently in the early stages there is a pronounced leukopenia. Eleven counts were below 4000 and two were below 2000 (1700 and 1400, respectively). As a rule, the patients who exhibited leukopenia on admission were sicker than those with a higher white-cell count. They showed a gradual increase in the white-cell count as the disease progressed. There were 9 cases with counts of over 25,000.

On admission the average percentage of polymorphonuclear leukocytes was 39. Later this fell to between 20 and 25 per cent. The disappearance of these cells may be alarming. Nine cases showed 15 per cent or less, and 1 showed only 4 per cent. The increase in mononuclear cells, which was both relative and absolute, roughly paralleled the clinical course.

Other abnormalities noted in the smears in 9 per cent of the cases included basophilic stippling of the erythrocytes and young forms of the polymorphonuclear series, which in 1 case had led to an earlier diagnosis of leukemia.

The necessity for taking frequent blood smears should be mentioned. It is not unusual to find the white-cell count relatively normal early in the disease and to note a change after the patient has apparently recovered.

The development in 1932 of the diagnostic test by Paul and Bunnell⁴—variously known as the sheep-cell agglutination test, the heterophil-antibody test and the Paul-Bunnell test—has provided a valuable diagnostic aid. This relatively simple procedure is a measure of the ability of the serum to agglutinate washed sheep erythrocytes in increasing dilutions of serum. The titer thought by most investigators to be diagnostic is 1:64.

One or more agglutinations were performed in 95 cases of the combined series. A positive reaction was present in 86 (90 per cent). In the 9 cases in which the reaction was negative and in the remaining 16 cases, blood smears and clinical findings were so typical that repeated tests would no doubt have given positive reactions. In many of the cases that finally showed a positive reaction, negative or low titers were encountered early in the course of the disease. On the other hand, one patient on the second day after admission had a positive agglutination reaction in a dilution of 1:114,000, and on the twelfth day this was still positive in a dilution of 1:7000. This patient was a moderately allergic person who had had no recent injections that could have accounted for such a titer of antibody.

No case had a history of recent serum disease, the only other common process that produces a positive heterophil reaction. One case had been diagnosed elsewhere as brucellosis and had been treated with injections of brucella. The brucellar

agglutination that was positive in a dilution of 1:160, whereas the heterophil test was positive in a dilution of 1:896. The blood smears were typical of infectious mononucleosis.

Positive agglutination reactions for typhoid and paratyphoid B bacilli in a dilution of 1:160 were found in still another patient, in whom the diagnosis was for some time obscure. This peculiarity of the serum of patients with infectious mononucleosis has been noted by other investigators and may, unless recognized, make matters confusing for the physician.

COMPLICATIONS

Besides the previously mentioned cases of peritonsillar and lingual abscess, there were various other complications in this series.

One patient developed acute purulent otitis media on the fourth hospital day, which responded to paracentesis and chemotherapy. Although cough was a frequent symptom, only 1 case showed bronchopneumonia. Another patient, however, had been in Dick's House for sixteen days because of infectious mononucleosis and had made an apparently normal recovery. He was readmitted eight days later because of findings suggestive of atypical or virus pneumonia and died on the eleventh day. It was in this case that the polymorphonuclear count dropped to 4 per cent, although by the time of the second admission it had risen to 52 per cent.

None of the patients who complained of abdominal pain presented the clinical picture of acute appendicitis. Except for 1 case, there was no major gastrointestinal complication. This patient, who was moderately sick, had several episodes of hematemesis over a twenty-four-hour period. Tarry, guaiac-positive stools were found for several days thereafter. He improved promptly on general supportive measures, and no specific cause for this striking manifestation was ever discovered.

Perhaps the most unusual complication in the series was that of a nineteen-year-old student who in February, 1936, was admitted to Dick's House shortly after falling and injuring his left side in a skiing accident. Prior to this, he had been in apparently good health. On admission, he complained of pain in the left upper quadrant of the abdomen, radiating to the left shoulder. Examination showed the typical findings of a ruptured spleen. The white-cell count was 4250, with 89 per cent mononuclear cells. After transfusion, an exploratory celiotomy was done. A large spleen weighing 970 gm and with a jagged laceration was removed. The postoperative course was stormy, being complicated by atelectasis and pneumonia, but the patient eventually made a normal recovery. The preliminary diagnosis from the microscopic sections was lymphoblastoma of the Hodgkin's type, but the blood smears, re-examination of the spleen by several pathologists and the subsequent course

have borne out the diagnosis of infectious mononucleosis. At present, the patient is in excellent health. Rupture of the spleen in infectious mononucleosis has been reported previously.

Lymph-node biopsy is rarely either necessary or helpful in infectious mononucleosis. In a patient who entered with complaints of pain in the left upper quadrant of the abdomen and low-grade fever and in whom axillary and inguinal lymphadenopathy and splenomegaly were found, an inguinal node was excised for diagnosis. Microscopic examination showed a normal node. The patient subsequently developed jaundice and was seen in consultation by Dr William P. Murphy. The diagnosis of familial hemolytic jaundice was entertained until the late appearance of several strongly positive heterophil reactions. The patient had a protracted convalescence and after eight months still had a palpable spleen.

Tachycardia, an admission complaint in 2 cases, disappeared on bed rest. No other cardiac complications were discovered, and further study of these cases showed no abnormality. Urinary complications, except for transient albuminuria, were not seen.

Although not a complication in the usual sense of the word, persistent fatigue or weakness and inability to regain former endurance was a feature in many cases. Three patients were readmitted because of a relapse or persistence of symptoms. One, a nurse, was hospitalized three times.

LENGTH OF HOSPITALIZATION

The number of days spent as inpatients was similar in both groups, averaging 13.1 days in the infirmary and 11.4 days in the hospital. The shortest time for either was two days, and the longest was thirty-six days in the hospital and forty days (2 cases) in the infirmary. Eighteen patients were hospitalized for over twenty days. The nurse mentioned above aggregated forty-two days for her three admissions.

The duration of hospitalization is not a fair estimate of the duration of illness, for many patients were dismissed to their homes for convalescent

care, and the first hospital day usually came some time after the first day of the illness.

TREATMENT

With the etiology of infectious mononucleosis unknown, there can be no specific therapy. Intelligent handling and the use of general measures is adequate for the average case. Sore throat was treated by saline-solution irrigations, and pain was controlled by codeine and aspirin. Mouthwashes or gargles with sodium perborate were useful in cases with Vincent's infection. Their routine use seems worth while in preventing gum involvement. Neoarsphenamine was rarely used and appeared to produce no dramatic results. Sulfadiazine had no appreciable effect on the disease.

Cases in which vomiting, diarrhea, sweating or dysphagia seriously upset the fluid and electrolyte balance profited by parenteral fluids.

SUMMARY

The history and clinical findings in two groups of cases of infectious mononucleosis, occurring at the same time and treated by the same physicians, are discussed, and significant features are described.

Infectious mononucleosis is a fairly frequent, usually benign disease and is most frequently seen in young adults.

The diagnosis of infectious mononucleosis may be simple or obscure. A high degree of suspicion, not only in cases with symptoms suggestive of the usual upper respiratory infections but those resembling typhoid fever, leukemia, brucellosis, Hodgkin's disease, nephritis and infectious jaundice, will lead to the hematologic and serologic studies necessary to establish such a diagnosis.

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Correction In the paper "The Rehabilitation of Patients Totally Paralyzed Below the Waist With Special Reference to Making Them Ambulatory and Capable of Earning Their Living. I. Anterior Rhizotomy for Spastic Paraplegia" by Dr. Donald Munro, which appeared in the October 18 issue of the *Journal*, the word "SPIRAL" in the heading in the first column on page 454 should be changed to "SACRAL."

MEDICAL PROGRESS

HEMOGLOBINEMIA AND THE HEMOGLOBINURIAS (Continued)*

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PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

Paroxysmal nocturnal hemoglobinuria, the strangest of this entire group of bizarre diseases, is also the most infrequent. Only 50 cases have been reported since Marchiafava and Nazari⁶⁰ first recognized the condition as a separate disease entity in 1911. The disease usually appears during the third or fourth decade of life, although it has been described in a child of five and a half years⁶¹ and a woman aged fifty-two years.⁶² Of the reported cases, 25 have been males and 25 females. There is no demonstrable hereditary or familial tendency, and careful studies have failed to reveal predisposing diseases or etiologic factors of any type. The victims of the disease usually have been perfectly well prior to its onset, which may be insidious, with gradual progression of symptoms for several years, or abrupt, with the sudden onset of massive hemoglobinuria. The hemolytic process at first may be so mild that the only symptoms are those of hemolytic anemia and hemoglobinuria may not develop until years later.⁶³ Once established, the disease is remarkable for its chronicity, its spontaneous remissions and exacerbations and its refractoriness to all therapeutic measures. Although cases have been observed for as long as thirty-three years,⁶⁴ no case of complete recovery has been recorded. The clinical picture is one of persistent and marked chronic hemolytic anemia with superimposed exacerbations, during which the hemolytic process is accelerated and hemoglobinuria appears. In the intervals between exacerbations, anemia is always present, with its associated symptoms of weakness and easy fatigability. Hemoglobinemia can always be demonstrated, and mild jaundice is frequently noted. During the intervals between acute exacerbations patients usually are able to perform light work, and once they have become adjusted to their anemia they get on remarkably well.

Exacerbations occur at irregular intervals and usually without obvious cause, although the onset of any infection, no matter how mild, may precipitate an attack. Exertion and exposure to cold neither precipitate nor aggravate attacks. They may occur at frequent intervals, or rarely, many months or several years⁶⁴ may intervene between attacks.

Each attack may persist for only a few days or may last for several weeks. With the onset of an exacerbation, the hemolytic process increases in severity, anemia becomes more marked, hemoglobinemia rises and hemoglobin appears in the urine. During these attacks the patient usually is markedly prostrated and completely incapacitated. Chills and fever may occur, vague aches and pains are noted, and severe cramping abdominal and lumbar pains are occasionally present. The spleen and liver are frequently moderately enlarged and may vary in size from time to time.

One of the most striking features of the disease is the nocturnal character of the hemoglobinuria. During the daytime waking hours the urine may be completely free of hemoglobin, but at night and shortly after waking in the morning the urine may contain so much hemoglobin that it is absolutely black in color. As subsequently noted, this apparent diurnal variation in hemoglobinuria is really a reflection of the sleeping and waking habits of the patient, the actual cause of the increase in hemoglobinuria at night being associated with increased hemolysis occurring during sleep.

Venous thromboses have occurred in approximately one quarter of the reported cases and constitute the most serious complication of the disease. They usually develop during the acute exacerbations but also have been observed during periods of remission when there was no hemoglobinuria.⁶⁵ They most frequently occur in the portal system, with involvement of the mesenteric veins and ensuing intestinal infarction.^{62, 66} Intracranial vascular occlusions with hemiplegia are also of fairly common occurrence.^{62, 66} Thromboses of the peripheral veins and pulmonary infarction also have been reported.^{63, 66-68}

Why thromboses are prone to develop in this disease has not been satisfactorily explained. Scott, Robb-Smith and Scowen⁶² have suggested that localized accumulations of erythrocyte stroma or agglutination of hemolyzing erythrocytes may produce vascular occlusion. Hjärre⁶⁹ demonstrated that injections of erythrocyte stroma into animals produced thromboses in the lungs and areas of focal necrosis in the liver — another lesion frequently encountered in paroxysmal nocturnal hemoglobinuria. It is possible that a similar mechanism is operative in paroxysmal nocturnal hemoglobinuria, but some other factor is probably present as well, since other types of hemolytic anemia are not characteristically associated with thrombotic manifestations.

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Free hemoglobin is constantly present in the blood plasma of patients with paroxysmal nocturnal hemoglobinemia, although its concentration may be below the renal threshold and none may be present in the urine. When the total concentration of heme pigments is in excess of 250 to 300 mg per 100 cc, methemalbumin appears and may be detected spectroscopically. Plasma bilirubin always is increased and, following excessive hemolysis, may reach levels of 5 or 6 mg per 100 cc, with associated jaundice.

In addition to these signs of increased blood destruction, there is also evidence of an increased rate of blood regeneration. reticulocytosis is constantly present during periods of exacerbation and may reach levels of 20 or 30 per cent. The bone marrow shows increased erythropoietic activity, with hyperplasia of erythroblastic elements.⁶² In spite of the marked reticulocytosis and increased blood regeneration, the rate of blood destruction is always in excess of blood formation, and a marked anemia is constantly present. As a rule, the red-cell count varies between 2,000,000 and 3,000,000, but a value of 1,000,000 is frequently encountered and it rarely rises to 4,000,000. The erythrocytes are moderately macrocytic, and the mean corpuscular hemoglobin concentration is normal. They show a normal resistance to hemolysis by hypotonic solutions of sodium chloride, and the Donath-Landsteiner test for cold hemolysins is negative.

Diagnostic of this disease is the increased susceptibility of the red blood cells to hemolysis by acidified plasma. This abnormality was first noted in certain cases of hemolytic anemia by Van den Bergh,⁷⁰ but he did not succeed in distinguishing the disease entity of paroxysmal nocturnal hemoglobinuria from other forms of hemolytic anemia. Ham^{71, 72} and Dacie, Israëls and Wilkinson⁷³ recently reinvestigated the sensitiveness of these erythrocytes to increased acidity. Ham's studies have placed the so-called "acid hemolysis test" on a sound basis and have done much to clarify the pathologic physiology of the disease. He found that marked hemolysis was produced when the patient's erythrocytes were mixed with blood serum obtained either from the patient or from a normal control subject and when the acidity of the mixture was increased to pH 6.8 or 7.0 by equilibration with carbon dioxide or by admixture with a small amount of mineral acid. Normal control erythrocytes showed no or minimal hemolysis when similarly treated. These studies indicated that the fundamental abnormality resided in the erythrocytes but did not exclude the possibility that the cells might have been sensitized by absorption of some hemolysin. Subsequent investigations revealed no plasma hemolysin or antibody of any type but did demonstrate that a constituent of normal plasma was essential for the production of hemolysis, even in acid mediums.⁷⁴ This plasma was extremely thermolabile, being de-

stroyed by exposure to a temperature of 56° C for five minutes, and it was concluded that it was closely associated with, if not indistinguishable from, complement or alexin. In contrast to the hemolytic system existing in cold hemoglobinuria, the hemolytic activity of the inactivated serum could not be restored by the addition of guinea-pig complement.

Although the increased susceptibility of erythrocytes to acid hemolysis is a characteristic feature of paroxysmal nocturnal hemoglobinuria that has been confirmed by numerous investigators, it is questionable whether a similar mechanism operates to produce intravascular hemolysis in patients with disease. Ham⁷² clearly demonstrated that the nocturnal character of the hemoglobinuria was merely a reflection of the fact that hemolysis is accentuated and hemoglobinuria occurs during sleep. By causing patients to sleep during the daytime and stay awake at night, hemoglobinuria could be made to appear during the daytime, while the urine was free from hemoglobin during the night. By preventing sleep for many hours, hemoglobinuria was eliminated, only to recur as soon as the patient went to sleep. Ham attempted to correlate these observations with the slight decrease in the alkalinity of the blood that is stated to occur during sleep.⁷⁵ Pulmonary ventilation decreases during sleep, and there is a consequent slight increase in the carbon dioxide content of arterial blood, with a resultant decrease in the alkalinity of the plasma. These changes seldom, if ever, lower the reaction to pH 7.2, however, and in several carefully studied patients with paroxysmal nocturnal hemoglobinuria, it was impossible to demonstrate any change whatever in the reaction of the blood during sleep.^{72, 76} Ham has suggested that the reaction of the blood in the viscera may fall to levels low enough to produce marked hemolysis, but there is no experimental support for this hypothesis. There is no doubt of the fact that, *in vitro*, a slightly acid blood plasma produces hemolysis of the erythrocytes in the presence of human complement. Whether this mechanism operates *in vivo* is still open to question. At present, no better hypothesis than Ham's has been advanced. A somewhat analogous situation exists in familial hemolytic jaundice: the erythrocytes in this disease show an increased susceptibility to hemolysis by hypotonic solutions of sodium chloride, and yet there is no evidence that any condition of hypotonicity exists *in vivo* to account for the increased hemolysis in patients with this disease.

Leukopenia and thrombocytopenia are characteristic features of paroxysmal nocturnal hemoglobinemia. The white-cell count is usually between 2000 and 4000, and the differential count is relatively normal or shows a relative lymphocytosis. The leukopenia may contribute to the susceptibility and poor resistance of these patients to infections, al-

though during acute infections the leukocyte count often rises to high levels⁶⁵ The blood platelets are markedly reduced in number, usually ranging between 100,000 and 150,000 per cubic millimeter Several cases have shown hemorrhagic tendencies, which are probably attributable to the thrombocytopenia^{61, 62, 77} Following splenectomy, the number of leukocytes and platelets may increase to normal, but occasionally severe leukopenia and thrombocytopenia persists indefinitely⁶⁶

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At autopsy, patients who have succumbed to paroxysmal nocturnal hemoglobinuria are found to have a characteristic distribution of iron-containing pigment in their tissues, a distribution that is found in no other disease entity The kidneys are described as "snuff-brown"⁸² or mahogany in color, and the Prussian blue reaction for iron-containing pigment is strongly positive in the cortices and interpyramidal substance but negative in the pyramids The reaction is also negative when applied to the liver and to the spleen. Histologic examination reveals large amounts of iron-containing pigment, presumably hemosiderin, in the epithelial cells of the renal tubules but none elsewhere. In the proximal convoluted tubules the hemosiderin is small in amount and finely dispersed, in the ascending loops of Henle and in the distal convoluted tubules, large amounts of iron are present in coarse granular aggregates Examination of the liver, spleen and bone marrow shows either no iron or a less than normal amount This distribution of iron in the tissues is peculiar to paroxysmal nocturnal hemoglobinuria In other forms of chronic hemolytic anemia, for example, familial hemolytic jaundice, the liver, spleen and bone marrow, as well as the kidneys, contain large amounts of iron In hemochromatosis, iron is deposited in the adrenal cortices, the testes and the skin, in addition to the spleen, liver and kidney

The unusual distribution of iron in these cases is readily explained by a consideration of the pathologic physiology of hemoglobinemia and of iron metabolism in anemia The persistent hemoglobinemia results in an almost constant leakage of hemoglobin through the glomerular membrane into the glomerular filtrate As a consequence, tubular epithelial cells must constantly be reabsorbing hemoglobin, breaking it down to hemosiderin and returning it to the hematopoietic system for reuse in the manufacture of new hemoglobin This explains why deposits of iron are readily demonstrated in the tubular epithelial cells and why there is a persistent hemosiderinuria When these cells become "loaded" with hemosiderin they may be dislodged and excreted in the urine In contrast to the situation in the kidneys, the chronic anemia and the constant demand for iron for hemoglobin synthesis results in a steady drain on the usual sites of iron storage These tissues consequently contain less than their usual complement of iron

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and urine by the administration of sodium bicarbonate and other bases. Although transient benefit has been reported in some cases,^{72, 76} hemoglobinuria soon reappeared and exacerbations were likely to be much severer than when alkalis had not been administered. Frequent feedings during waking and sleeping hours with the hope of producing an alkaline urinary tide have not been beneficial.^{72, 77} Injections of sympathicomimetic and parasympathicomimetic drugs have been reported to be of value by Hoffman and Kracke,⁷⁶ but the effects obtained are far from clear cut.

Splenectomy has been performed in many cases of paroxysmal nocturnal hemoglobinuria, always without benefit, and numerous fatalities have resulted from the effects of the operation.

Blood transfusions used as a supportive measure when anemia is extreme have definite but transient therapeutic value. Patients with paroxysmal nocturnal hemoglobinuria are prone to develop severe pyrogenic reactions after transfusions with compatible blood, and hemolysis of the patient's own erythrocytes may be greatly accentuated after transfusion. Thromboses may also occasionally occur during or after transfusion. In spite of these hazards, however, it is necessary to transfuse some patients at fairly regular intervals to combat the anemia, which otherwise becomes so extreme that it completely incapacitates the patient.

Although transfusion of blood may temporarily aggravate the hemoglobinuria, a definite remission of the hemolytic process often occurs and the urine may remain free from hemoglobin for a period of weeks or months following the injection of the blood.^{66, 82}

In summary, there is no specific therapy for paroxysmal nocturnal hemoglobinuria, but with careful medical supervision and the judicious use of blood transfusions, patients with this disease can lead useful lives for many years. Operative procedures of all types, especially splenectomy, are to be avoided, and any infection, no matter how slight, should be immediately controlled.

BLACKWATER FEVER

Certain cases of falciparum malaria are complicated by acute hemolytic anemia, hemoglobinemia and hemoglobinuria, a syndrome recognized for centuries and commonly known as "blackwater fever." The syndrome occurs most frequently in Europeans who have resided several years in highly endemic malarial regions and who have experienced several attacks of falciparum malaria. The disease is usually precipitated by medication with quinine,⁸³ atabrine⁸⁴ or plasmoquine,⁸⁵ and is characterized by rigor, fever, vomiting, jaundice and the passage of black urine containing large amounts of hemoglobin. Prostration and extreme weakness are outstanding features of the disease and are a reflection of the rapidly progressing anemia produced by the exces-

sive hemolysis. The number of erythrocytes may decrease to 20 or 30 per cent of normal within twenty-four to forty-eight hours, and the deleterious effect of this sudden and extreme anemia on the heart and vascular system may be so severe that the slightest exertion may precipitate sudden death. Blood destruction is occasionally so excessive that shock-like states develop and death may occur within a few hours.

Hemoglobinuria is intense and may persist for a few hours or several days. Black urine lasting for longer than twenty-four hours is of grave prognostic significance.⁸³ Some patients develop oliguria, anuria, and uremia following the hemoglobinuria, a sequence of events almost always leading to death regardless of therapeutic measures.

Treatment of the syndrome is limited to supportive measures, which must be instituted as soon as evidence of increased hemolysis is apparent. Warmth, maintenance of adequate fluid and electrolyte intake, sedation and absolute bed rest must always be provided. Victims must not be moved until the acute episode is over, because of the danger of precipitating sudden death from fibrillation of the weakened cardiac ventricle. Blood transfusions should be administered if the anemia is rapidly progressive or of extreme severity. Transfusions are of considerable benefit in the majority of cases, although the transfused cells are apparently hemolyzed just as readily as the patient's own erythrocytes.⁸⁶

Antimalarial drugs should be administered to patients with blackwater fever only if there is unmistakable evidence of heavy parasitization of erythrocytes, an occurrence which is very infrequent.⁸⁷ Some authorities warn against giving antimalarials at any time during the acute course of the disease since it has been suggested that these drugs aggravate the hemolytic process.^{88, 89} Foy and Kondi,⁹⁰ from experience gained from 450 cases of blackwater fever in Macedonia, advise cautious administration of quinine or atabrine if parasites are particularly numerous and if malarial paroxysms are superimposed on the symptoms of blackwater fever.

Since the investigations of Baker and Dodds²¹ indicated that an alkaline urine might prevent the formation of acid hematin casts in the renal tubules, it has been standard practice to attempt to alkalinize the urine of blackwater-fever patients. Although recent authoritative publications^{24, 89} still recommend the administration of alkalis until the urine becomes alkaline, careful consideration of experimental and clinical evidence gives little support to the belief that alkalization changes the course of the disease or decreases the number of fatalities.²⁴ Large quantities of alkali may actually be harmful, since they tend to upset further an already disturbed acid-base balance and produce alkalosis of severe degree. In the administration of fluid

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known hazard in these exercises to introduce a second diagnosis when one can explain the picture on the first one. In the face of that danger, my guess is that this was not a recurrence of the carcinoma.

If it was something else, what was it? The chances are that he had an obstruction either from a new tumor or from a stone. Which of those is it going to be? Here again his general condition was exceedingly good for a man with carcinoma of the head of the pancreas, carcinoma of the ampulla or carcinoma of the bile duct. He had some pain with the onset, but the nature of the attacks of pain does not help me much. The pain was on the left side, which is wrong for the gall bladder, and I do not know quite what to make of it. He had had a mild diabetes for some time. What bearing did that have on the picture? It probably had none. The incidence of gallstones in diabetic patients is slightly higher than that in normal people, which might make the statistical probability of gallstones greater, but other than that I do not believe that it had any bearing.

The laboratory data, except for revealing a normal hemoglobin and white-cell count, do not help me much. The problem, to my mind, comes down to a guess between a stone obstructing the ducts or a tumor, probably a new one if it was a tumor. Because of the fairly short duration of the illness and because of the patient's good general condition I think that the chances are a little better that in this case we are dealing with an obstructive jaundice on the basis of a stone.

DR. RONALD C. SNIFFEN: Dr. Herrera performed a peritoneoscopy before operation. What did you find, Dr. Herrera?

DR. RODOLFO E. HERRERA: The main reason for performing the peritoneoscopy was to rule out metastatic carcinoma from the rectum. We believed, as Dr. Bartlett did, that this man probably had a new disease, but because we had recently had two patients with jaundice who had returned to the hospital with widespread liver metastases from carcinoma of the breast but who had not shown evidence of weight loss, a peritoneoscopy was done. In this case we found that the liver was a bit enlarged and had a greenish-yellow tinge, which was consistent with obstructive jaundice. There were no implants in the peritoneum. The gall bladder was rather large. It did not appear thickened or tense when touched with the tip of the peritoneoscope, and there were no adhesions around it to suggest that he had had previous attacks of cholecystitis. We thought that he had an obstructive jaundice, but it was impossible to tell whether he had a new growth, enlarged lymph nodes in the region of the common duct or stone. At any rate no tumor could be seen in the region of the head of the pancreas.

DR. SNIFFEN: Are there pertinent x-ray films?

DR. CLAYTON H. HALE: The films do not contribute much. The colon was not well prepared and shows defects that are probably fecal material. No studies of the upper gastrointestinal tract were done. The chest shows no evidence of metastatic disease.

DR. JOSEPH C. AUB: How can a man who is deeply jaundiced have a normal urine? "Normal" is a dangerous word in medicine. It usually means that you do not find anything positive that you test for.

DR. SNIFFEN: We made an unintentional omission in our abstract of the clinical history. The urine showed a ++ test for bile.

CLINICAL DIAGNOSIS

Obstructive jaundice

DR. BARTLETT'S DIAGNOSES

Stone in common bile duct

Obstructive jaundice

ANATOMICAL DIAGNOSES

Stone at bifurcation of common hepatic duct.

Bile stasis of liver

Aspiration pneumonia

PATHOLOGICAL DISCUSSION

DR. SNIFFEN: The operation was performed five days after the peritoneoscopy. The surgeon found a distended gall bladder containing stones and removed it. The common duct was then explored and found to be very narrow, although fine probes entered the duodenum. Fine probes could also be inserted into the right and left hepatic ducts. The head of the pancreas seemed normal. The duodenum was then opened and the ampulla visualized and palpated, but it, too, was normal. Post-operatively the patient did not do well. He was treated with intravenous fluids, transfusions and Hykinone. The bile coming from the catheter in the common hepatic duct was normal in appearance, but the average daily output was only 100 cc. His death seemed to be due in large measure to the sudden aspiration of a large amount of stomach contents.

At the time of death the patient was severely jaundiced. The operative field was in good condition, and there was gastric dilatation. The lungs were heavy; there was consolidation in both lower lobes, and gastric contents in the trachea and bronchi. The liver was dark green to brown and enlarged, weighing 2650 gm. The intrahepatic and extrahepatic bile ducts were not appreciably dilated. A rubber catheter had been inserted into the bile duct at the point of entrance of the cystic duct, and its tip lay at the bifurcation of the common hepatic duct. Scattered in the small intrahepatic bile radicles there were calculi that resembled grains of sand. Straddling the bifurcation of the common hepatic duct and lying against the tip

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 31501

PRESENTATION OF CASE

A sixty-five-year-old man entered the hospital complaining of jaundice.

About three months before admission he first noted transient attacks of mild pain in the left upper quadrant of the abdomen. These attacks increased in frequency and severity. They often came on after meals but were not attributed to any particular type of food. Three weeks before admission he noticed the onset of increasing jaundice, without pain. The stools were clay colored and more frequent than previously. During the development of the jaundice the urine was dark red. During the week before admission he was nauseated and vomited once. The appetite had been good. He had lost about 3 pounds in weight since the onset of the illness.

The past history revealed that two years before admission the patient had undergone a combined abdominoperineal resection of the rectum for carcinoma. His health after this operation had been good until the onset of the present illness. For a number of years he had had mild diabetes, which was easily controlled by small doses of insulin.

On physical examination the patient was well developed and nourished. The skin and scleras were deeply jaundiced. The eyes were slightly prominent. The pupils did not react to light, the left pupil measured 2 mm in diameter, the right 3 mm. The heart was not enlarged. A Grade I systolic murmur was heard at the apex. Except for increased breath sounds over the right lower lobe the lungs were normal. The abdomen showed a functioning, well healed colostomy, a midline suprapubic scar and a cecostomy scar. The liver was palpable two fingerbreadths below the right costal margin, and its edge was irregular.

The temperature was 98°F, the pulse 80, and the respirations 20. The blood pressure was 130 systolic, 70 diastolic.

The urine was normal. The red-cell count was 5,100,000, with 100 per cent hemoglobin. The white-cell count was 18,400, with 80 per cent neutrophils. The nonprotein nitrogen was 41 mg per 100 cc, and the total serum protein 5.92 gm, with

3.65 gm of albumin and 2.27 gm of globulin. A cephalin flocculation test was negative in twenty-four and forty-eight hours. The prothrombin time was normal. The serum bilirubin was 15.2 mg per 100 cc direct, and 20.5 mg indirect. The serum phosphorus was 2.8 mg per 100 cc, and the alkaline phosphatase 14.8 units. A blood Hinton test was negative.

An x-ray film of the chest taken on the second hospital day showed a large thorax and kyphosis of the dorsal spine. The lungs were clear, without evidence of metastatic lesions. Injection of barium through the colostomy on the seventh hospital day showed that the proximal colon contained a large amount of retained contents but no obstruction was visualized. Barium proceeded into the terminal ileum. Barium did not fill more than a small portion of the distal loop. An electrocardiogram showed normal rhythm, with a rate of 100. The axis was normal. The PR interval was 0.13 second. T_1 was flat, and T_2 and T_3 upright but low, the T waves in Lead CF_1 were upright, and those in Leads CF_2 and CF_3 inverted.

The patient was confused. He vomited frequently and received intravenous fluids. The diabetes remained under control.

On the eighth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. MARSHALL K. BARTLETT: As a starting point it seems to me that we can assume this is a case of obstructive jaundice. All the information points in that direction. It had been going on for three weeks and increasing fairly rapidly, so that on admission the patient had a serum bilirubin of over 15 mg. There was a history of clay-colored stools, and although there is no record of a stool examination to confirm that, I think that we must accept the history and assume that he had little, if any, bile in the intestinal tract. Attacks of pain are mentioned in the history, but they are not given much prominence and nothing is said about pain after he entered the hospital. I assume he had had no further attacks.

Here is a man who had had carcinoma of the rectum two years previously. Was the picture on entry a result of that or was it due to a new disease? If he had had enough metastatic disease to cause this marked degree of jaundice and obstruction to his biliary tree, it seems to me that he ought to have had more to show for it than he had. He had lost little weight, the red-cell count and hemoglobin were normal, and the chest film was negative, or at least showed no evidence of metastases. It seems to me unlikely that this is a picture of metastatic carcinoma from a lesion in the rectum. Of course, he could have had a small area of metastatic disease obstructing the biliary tree. I see no way to rule it out, but I think that it is unlikely. It is a well

cancer. The adjective "papillary" is used once, but otherwise the lesion is described as an ulcer that was soft, without an indurated edge. And after nine months there were no metastases in the cervical nodes. Cancer of the tongue can, I understand, rarely metastasize to the lungs. I have never seen a case, but I doubt that the lungs would give an x-ray picture like this. And while we are considering metastatic lesions of the lung, this is a good time to point out that, if the primary cancer

That brings us to tuberculosis. The lesion of the tongue is consistent with a tuberculous ulcer. It is true that in the cases that I have seen—and they have been few—there was reasonably severe pain and tenderness. But this man was an alcoholic addict, and much of his pain may have been dissolved in alcohol. One cannot count too much on his statements. I shall therefore accept the diagnosis of a tuberculous ulcer of the tongue. The chest film, with its diffuse shadows, and what I



FIGURE 1.

is in the testis, metastases to the lung usually give a snowball appearance and not such diffuse shadows as are apparent here. Metastatic malignancy from the stomach or pancreas may give an x-ray picture much like this, except that there is almost never a cavity at the left apex, which is, I believe, pictured here. So the x-ray film of the chest seems to me to be much more characteristic of another diagnosis than it is of malignancy. I am ready to dismiss cancer of the tongue and metastatic disease of the lung, but I must consider cancer again in speaking of the genitourinary tract.

believe to be a cavity at the left apex, seems more like tuberculosis than anything else. No sputum examination is reported, and one examination of the gastric contents is reported not to have shown acid-fast bacilli. Nevertheless, I believe that this man had pulmonary tuberculosis.

Finally we must consider the lesions in the prostate and testis. The firm, fixed lesions described could, it seems to me, be due either to cancer or to tuberculosis. I admit that tuberculosis of the testicle without associated involvement of the epididymis is unusual, but I assume that there was at least some

of the catheter there was a stone that measured 12 mm in length and 6 mm in diameter. It lay transversely, so that both right and left hepatic ducts were blocked. This stone was loosely held together, and when one picked it up with forceps, it was devoid of substance and felt like soft tissue. Furthermore it did not seem to be impacted in its position. I imagine that it rocked back and forth as the probe was inserted into the hepatic ducts. The kidneys were swollen and green. The tubules contained bile casts, and some of the cells of the convoluted tubules were undergoing degeneration. The interstitial tissue was edematous and infiltrated with mononuclear cells.

No metastatic tumor could be found.

CASE 31502

PRESENTATION OF CASE

A forty-eight-year-old stockbroker entered the hospital complaining of an ulcer of the tongue.

Nine months before admission the patient noted a painless ulcer on the undersurface of the tongue near the tip. It reached a diameter of about 1 cm and then remained stationary up to the time of admission. A blood Wassermann test was negative. Treatment with potassium iodide caused no change in the lesion. Six months before admission a painless left testicular mass was found, which had not increased in size.

The past history revealed that the patient had been a heavy user of alcohol for many years, often consuming as much as one quart of hard liquor a day. He had never had hallucinations but was troubled with tremor.

On physical examination, the patient was well developed but thin and pale. He was apprehensive. A coarse tremor shook his body, and he was unable to stand or walk. The skin and lips were dry and scaling. The tongue was beefy red, with a smooth border. It showed a coarse tremor. On the underside of the tip, to the left of the midline, was a circular, papillary, yellowish-gray lesion 1 cm in diameter. It was well circumscribed, nontender and soft. There were no other lesions in the mouth. The cervical lymph nodes were not enlarged. Breath sounds were increased over both apices, and there was decreased resonance throughout. No rales were heard. There was a soft systolic murmur in the left second interspace. The abdomen was moderately tender in the right upper quadrant and slightly tense throughout. The left testis was enlarged to form a firm, irregular, nodular, nontender mass, measuring 4 by 2 cm. It did not transilluminate. Rectal examination revealed a soft, lobulated, slightly tender, right prostatic lobe, measuring 6 by 3.5 cm, the left lobe was extremely firm, fixed and 2.5 cm in diameter. The reflexes were normal.

The temperature was 101°F, the pulse 100, and the respirations 20. The blood pressure was 80 systolic, 70 diastolic.

The urine was normal except for a + test for diacetic acid. The red-cell count was 4,200,000, with 10.4 gm of hemoglobin. The white-cell count was 5000. The nonprotein nitrogen was 13 mg per 100 cc, and the serum chloride 80 milliequiv per liter. The total serum protein was 5.4 gm per 100 cc. A smear of gastric contents was negative for acid-fast bacilli.

A chest film showed mottled density throughout both lung fields, more marked in the upper than in the lower portions (Fig. 1). A bleb or cavity was present at the left apex. The diaphragm was normal in position. The costophrenic sinuses were clear. The heart and upper mediastinum were not remarkable. A flat film of the abdomen showed distention of loops of small intestine and gas in the large intestine as far as the splenic flexure. An intravenous pyelogram was unsatisfactory. The bladder was small and contracted.

During the hospital course, the patient's temperature fluctuated between 99 and 103°F, rising terminally to 106. He was disoriented and restless. He refused food and was given fluids intravenously. Lumbar puncture yielded a clear, colorless fluid. He expired on the ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. DONALD S. KING. In summary, we have a forty-eight-year-old patient who was suffering from chronic alcoholism, with marked vitamin B deficiency and so-called "alcoholic neuritis." Besides that he had lesions in four organs: the tongue, the lungs, the prostate and the testis. The anemia, low serum protein, low chloride and low blood pressure can be explained largely on the basis of the alcoholic history and are not, I believe, concerned in the diagnosis.

What disease or diseases may give lesions in the four organs named? One thinks first of the old trio: syphilis, cancer and tuberculosis. The choice in this case seems easy, but it is often these apparently simple cases in which we find a catch. So let us try to apply each of these three diagnoses to the lesions as described in the tongue, lungs, prostate and testis.

The first possibility is syphilis. There was one negative Wassermann test. The patient was given potassium iodide, and the tongue lesion did not change. He could have had a gumma of the testis and associated gonococcal infection of the prostate. Syphilis of the lung can occur, but the only cases in this hospital that we believe were proved were gummas, and the x-ray appearance was quite different from that shown here. I am ready to drop syphilis from the list.

The next possibility is cancer. The description of the lesion of the tongue is not characteristic of

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RESIDENCIES FOR DISCHARGED MEDICAL OFFICERS

THE last ten or fifteen years have witnessed a marked increase in the trend toward specialization in medicine. This has been considerably intensified by the creation of certifying boards in the many different specialties. Whether or not this trend is desirable or should be encouraged, it has had the effect of essentially adding another three or four years of postgraduate training to the already long time that it takes until physicians are prepared to enter the practice of medicine.

On the larger and better hospitals, particularly those in the big medical centers of this country and those attached to medical schools, has fallen the duty of providing this specialized training and of

maintaining the high standards of medical practice that make such training possible. Under normal conditions, it has usually been possible for these hospitals to provide for a number of men equal to between 15 and 30 per cent of those who enter preliminary training as interns immediately after they receive their medical degrees. To maintain some continuity, especially in hospitals where there are short or rotating internships, it is usually necessary to choose largely from among those who received their earlier training in the same hospital. Since it is frequently desirable to inject the refreshing influence of men trained elsewhere, a small number may, under suitable circumstances, be taken from other hospitals. This often has the effect of temporarily reducing the efficiency of the hospital staff because the new persons lack acquaintance with their new environment, and in addition, it decreases the opportunities available to the men who received their early training at that institution. Furthermore, it is necessary to select men who are suited for the responsibilities entailed in the advanced positions. They not only must be able to direct the work of the interns but must also be equipped to teach both students and interns and to discharge important administrative responsibilities in the hospital.

Since the beginning of the war, men have been graduated from various medical schools at nine-month intervals and the vast majority of them have had to enter the service immediately after the completion of a nine-month internship. A few of them have had the opportunity to stay on for a second nine-month period in the so-called capacity of "resident," but actually their duties have been similar to those that constitute the latter part of the usual internship in a good hospital. An extremely small number have been permitted to stay on for a third nine-month period. Six classes of interns have already been graduated into military service in this manner, with the result that only a small percentage of these men have had more than nine months of civilian hospital training. Some of them have already been separated from military service, and most of them will be returning within the next year or two, and practically all of them will want further hospital training. In ad-

involvement of the epididymis in this case. So, having accepted tuberculosis as the diagnosis for the lesions of the tongue and lungs, I shall also accept it for the prostate and testicle. There is insufficient evidence for a diagnosis of tuberculosis of the intestines or central nervous system. I shall be interested in knowing whether the small contracted urinary bladder was due to tuberculosis of the bladder wall. I shall also ask the old question whether alcoholic cirrhosis was found.

In my own study of the record I had gone this far without looking at the x-ray films of the abdomen, which were given to me yesterday. Perhaps this preview gave me information that I should not have had. But I do not believe that it influenced my diagnosis, although I am willing to grant that it confirmed my suspicions.

DR CLAYTON H. HALE: This plain film of the abdomen shows dilated loops of small and large bowel, as described in the record. The bladder is rather small. I should say that it was characteristic of the contracted bladder of tuberculosis.

DR KING: The two things that I noticed were a mass of calcified abdominal nodes and a rounded calcified area, which I believe is in the left testis. If the mass in the left testis is calcified, it is a strong argument for tuberculosis. Do you think that the area in question is in the left testis?

DR HALE: It could be, I cannot be sure.

DR RONALD C. SNIFFEN: Dr. Nathanson, you saw this patient. Would you like to comment?

DR IRA T. NATHANSON: This man came to the Tumor Clinic with the complaint of an ulcer of the tongue, and it became apparent at the beginning that the lesion was an unusual one from the standpoint of diagnosis. The lesion appeared as described, it was papillary, yellowish gray and well circumscribed. We first thought that it was tuberculous, although it was not characteristic, as Dr. King has pointed out, of a tuberculous lesion of the tongue. Occasionally tuberculosis may be papillary or warty. The lesions that we have seen have been well circumscribed with sharp reddened edges, little or no induration and a yellowish base, and are usually tender, presumably due to secondary infection. There was surprisingly little or no induration. There were no lesions in the mouth that suggested vitamin deficiency, which occasionally causes an ulcer resembling this type of lesion. We were therefore unable to make a definite diagnosis but considered tuberculosis as one of the possibilities. The patient was put on potassium iodide to rule out the possibility of syphilis, even though the Wassermann test was negative. He was sent to the hospital for further study.

CLINICAL DIAGNOSIS

Pulmonary tuberculosis?
Carcinoma of prostate?

Carcinoma of tongue?

Carcinoma of testicle?

DR KING'S DIAGNOSIS

Tuberculosis of tongue, lungs, prostate, and testes

ANATOMICAL DIAGNOSES

Tuberculosis of tongue, epiglottis, larynx, lungs, testes, epididymes, prostate, bladder and left kidney

Mural thrombus left ventricle

Infarcts of spleen, right kidney and adrenal gland.

PATHOLOGICAL DISCUSSION

DR SNIFFEN: At the time of death the patient was quite emaciated. The ulcer on the undersurface of his tongue was 7 mm in diameter and had a ragged border and a dirty-gray base. The mucosa of the epiglottis and larynx was thick and hemorrhagic, with areas of ulceration. Each pleural cavity contained scattered fibrous adhesions but no fluid. The lungs were heavy and riddled throughout with firm, yellowish-white nodules from pin-head size to 3 cm in diameter. The intervening parenchyma was consolidated, and in some of the large nodules the tissue had broken down to form abscesses. Both epididymes and testes were matted together, fibrotic and riddled with abscesses, the enlargement was greater on the left than on the right. The prostate was large and almost destroyed by multiple abscesses. The left kidney contained nodules similar to those found in the lungs. All these lesions that I have described proved to be due to tuberculosis.

As an added insult there was a mural thrombus in the apex of the left ventricle. We could find no histologic reason for this, the underlying myocardium was normal, although the endocardium seemed to be destroyed at that point. Embolism, presumably from this mural thrombus, had produced infarcts in the spleen, right kidney and one adrenal gland.

The liver showed fatty change and central necrosis but no cirrhosis.

DR R. EARLE GLENDY: How about the urinary bladder?

DR SNIFFEN: It showed a tuberculous cystitis of the trigone where it was in contact with the prostate. There was, however, no mucosal ulceration.

DR GLENDY: Were there ulcers in the small bowel?

DR SNIFFEN: No.

DR MADELAINE BROWN: Did you examine the nervous system?

DR SNIFFEN: Yes. The brain was essentially normal, apart from an unidentified pigmentation around the substantia nigra. There were no changes indicative of pellagra.

DR BROWN: I do not suppose that you looked at the peripheral nerves.

DR SNIFFEN: Unfortunately, no.

tration and with the teaching of students and interns

Most medical schools and many hospitals have already completed plans that provide for the maximum number of men. Other hospitals are still groping with the problem and trying to increase the number of opportunities and to create new and desirable ones. Still others, which prior to the war had not had residents or even interns, are contemplating the establishment of facilities that will provide training of this type. In Massachusetts, all such plans are receiving the enthusiastic support of the Committee on Postwar Planning of the Massachusetts Medical Society. It is hoped that completion of these plans will not be too long delayed and that final details will be given adequate publicity. A large number of the returning men will undoubtedly have to content themselves with some type of refresher course designed to acquaint them with the best and most modern practices in medicine. Such courses should be suitable for some men who have already had two or more years of hospital training or who were already in practice before they entered military service.

DISABILITY DUE TO OCCUPATIONAL DERMATOSES

DISTURBANCES of the skin due to occupational factors have come to be recognized as a serious cause of disability among workmen at certain jobs. The relatively high incidence of such disturbances in general and in specific occupations is well known. The increase in the number of cases associated with war industries has been startling in certain industries. An article appearing elsewhere in this issue of the *Journal*, however, points out that little information is readily available regarding the toll that these diseases take in terms of compensation paid to the worker, the sums spent for medical treatment and hospital care or the duration of disability. The data that are available reveal how costly such conditions have become in the modern world of production and still more production. In the opinion of authorities in this field many of these losses are preventable, at least under peacetime conditions if full advantage is taken of the principles

of preventive medicine and the knowledge of corrective measures developed in the last few years, but it may take the full impact of the statistics of the end results and the costs of such disabilities to focus the requisite attention on these cases.

It is recognized, of course, that industrial accidents produce greater losses, but with occupational dermatoses accounting for 60 to 65 per cent of all occupational disease, their cost, figured in time and in dollars and cents, is a sizable one in the aggregate. It is true that many patients lose little or no time and have negligible expense, but there are numerous protracted cases and those in which the workman is unable to return to his former job, so that any stimulus to the investigation and prevention of such cases should produce benefits for both the employee and the employer. Although much has been learned about occupational dermatoses by the Office of Dermatoses Investigations of the United States Public Health Service and much has been accomplished in the way of their detection and prevention, the development of accurate statistics covering the losses resulting from such cases would without question stimulate a greater interest in them and their prevention.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

MOORE — George A. Moore, M.D., of Palmer, died October 6. He was in his seventy-fifth year.

Dr. Moore had been chairman of the board of trustees of the Monson State Hospital for a quarter of a century and had served as chief of staff of the Wing Memorial Hospital for the past fifteen years. He was a fellow of the American Medical Association and the American College of Surgeons and a member of the American Academy of Ophthalmology and Otolaryngology.

His widow, a sister and several nieces and nephews survive.

ZIELINSKI — Lieutenant Commander Ignatius Zielinski, U.S.N.R., formerly of Salem, died November 11 in a plane crash. He was in his forty-sixth year.

Dr. Zielinski received his degree from Tufts College Medical School in 1924. He was a surgeon on the Salem Hospital staff and had been medical examiner of the Tenth Essex district about ten years. He was a fellow of the American Medical Association. In the Navy, he first served at the dispensary of the Boston Navy Yard and later saw duty in Hawaii. He was assigned as chief surgeon to Quonset about a month ago.

His brother and five sisters survive.

MEDICOLEGAL ABSTRACT

Regulation of Practice by Government Qualification to practice Dr. Arnold Schleifer graduated from the University of Vienna Medical School on March 4, 1938. The Illinois State Department of Registration and Education at that time recog-

dition, many who previously had specialized training in certain fields will wish to return to similar positions because of their desire to continue in this specialty or to change to another. Perhaps a small percentage will be satisfied with a short period of refresher training before they enter or re-enter the practice of medicine.

Obviously, internships of the type that begin following graduation from medical school are not desired by the returning men. Possibly some of those who had only a short rotating service would like to have a straight internship in a teaching hospital. Those who do must, of course, compete with the men who are graduating from medical schools. It may be possible to increase to some extent the number of such internships, but it can hardly be expected that any significant number of desirable and acceptable appointments of this sort will be available to the returning servicemen.

The immediate and greatest demand will undoubtedly be for residencies, that is, for the equivalent of the second and third years of hospital training. As already indicated, such opportunities are normally offered only to one out of every five or six, or at most three, men after they have completed their first year of internship. Assuming that none of these places will be given to the men who are now finishing their internships, there will still be men equivalent in numbers to seven to nine medical-school classes who will be returning from military service within the next year or so. Should all these men apply for residencies, there would be somewhere between 21 and 54 of them competing for each place. Obviously, some expansion of opportunities can and will be arranged, but even these can hardly more than double the number of positions ordinarily available without defeating the entire purpose for which they have been or will be created.

All this bespeaks the unwisdom of the so-called "accelerated program," which was never adopted in Russia and was dropped after a short trial in Canada and Great Britain. The situation is disheartening to hospital administrators and to the chiefs of hospital services who are anxious to provide for the returning servicemen. It will appear even more discouraging to the latter, who, returning with high hopes of continuing their training, will find that the number of opportunities are even more

limited, relatively speaking, than they were under normal conditions. It will require a patient understanding on the part of those who are charged with choosing the men and on the part of those who are returning and seeking these positions. Obviously, a demanding attitude on the part of the veteran, based on his service record or on his rights and privileges, can only result in bitterness and

MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to:

George L. Schadt, *Chairman*
Postwar Loan Fund
8 Fenway
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disappointment. After all, the bulk of competition for the positions that these men seek will come from men who are in exactly the same situation that they are. Those who have the not-too-pleasant task of allocating the small number of places are already embarrassed at the idea of having to turn away so many men whom they would like to take and cannot.

Each hospital will eventually work out a solution that seems best suited to its peculiar circumstances. Obviously, each institution will feel that it owes some allegiance to its own graduates, particularly since they, like others, will be unable to find positions elsewhere. Even so, they still have the broader duty and obligation to encourage only those who are most suitable by their previous training, performance and personality. All these factors must be considered, since, as previously mentioned, residents must not only care for patients but also discharge duties concerned with hospital adminis-

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PENICILLIN AEROSOLIZATION IN THE TREATMENT OF SERIOUS RESPIRATORY INFECTIONS*

A Preliminary Report

MAURICE S. SEGAL, M.D. † AND CLAIRE MACINTYRE RADER, M.D. ‡

BOSTON

AEROSOLS may be defined as suspensions of liquids or solids in air or oxygen. The use of bronchodilator, vasoconstrictor and chemotherapeutic agents by continuous aerosolization with streams of oxygen or compressed air has been employed in patients with asthma,¹⁻¹⁰ pulmonary emphysema,⁴ pneumonia,¹¹⁻¹⁴ gas poisoning¹⁵⁻¹⁷ and other types of bronchopulmonary disease.^{13, 14} The value of such therapy can be appreciated if one recalls that the inner surface of the lung has an area five hundred times as great as the body surface and absorbs so rapidly as to give an effect similar to that of an intravenous injection. Furthermore, Krueger et al.¹⁸ demonstrated in monkeys and mice with India ink and with radioactive chromic phosphate as indicators, that with inhalation the material was uniformly distributed and penetrated to the outermost air sacs of the lungs at the ends of the bronchial tree. It is thus possible to obtain high local concentrations with varying blood levels via the pulmonary route.

The specific advantages of penicillin over the sulfonamides are as follows: its greater bacteriostatic power against streptococci and staphylococci, the slight effect on its action by the number of bacteria to be inhibited, its bacteriostatic power, which is not inhibited to any appreciable degree by products of tissue autolysis, *p*-aminobenzoic acid or pus, substances that generally annul the bacteriostatic action of the sulfonamides, and its nontoxicity. These advantages suggested to us its superiority as an aerosol in the treatment of serious respiratory disease.

Our earliest observations were made at the time of the Coconut Grove disaster in 1942. In 2 patients with inhalational pneumonitis 500 units of penicillin in 1 cc. of distilled water was given at

irregular intervals, with the small Vaponefrin nebulizer connected to the oxygen regulator. No accurate conclusions could be derived. Considerably later, when an adequate supply of penicillin could be obtained and proper nebulization equipment had been constructed, we were able to make more progress.

Within the past year, Bryson, Sansome and Laskin¹⁹ working largely with rabbits and normal human beings, demonstrated that penicillin aerosol particles are of sufficient physical stability and of a size favorable for therapeutic use. When inhaled the penicillin aerosol penetrated the lungs, diffused into the blood stream and was excreted in the urine. These authors concluded that a more uniform blood concentration can be maintained by the inhalation method than by intermittent intravenous or intramuscular injections. More recently Barach and his associates^{20, 21} have confirmed these observations in rats and in a series of 20 patients with infective bronchial asthma, bronchiectasis and lung abscess. The predominating organisms in the sputum culture were consistently absent for twenty-four hours after discontinuance of treatment. The penicillin blood level one hour following inhalation of the aerosol was generally between 0.01 and 0.04 Oxford units and at times as high as 0.10 units. They employed largely concentrations of 40,000 to 50,000 units per cubic centimeter of saline solution. In general, higher levels of penicillin in the blood were obtained after the larger doses. Other factors, such as the subject's breathing pattern, the degree of pulmonary fibrosis and the amount of prevalent expectoration, modified the penicillin blood level. It was further demonstrated that penicillin aerosol protects rats against systemic hemolytic streptococcus infection and that no pathologic irritant effects can be demonstrated in the lungs at post-mortem examination.

Olsen²² described the use of nebulized penicillin preoperatively and postoperatively in a series of 7 patients with surgical bronchiectasis and 8 patients

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‡Outpatient physician, Boston City Hospital.

nized the Vienna school as reputable and in good standing. Four years later it retroactively suspended recognition of the university, thus purporting to deprive Dr. Schleifer of the right to be examined to practice medicine in Illinois.

Dr. Schleifer brought mandamus to compel the director and the superintendent and others of the department to grant him access to the examination of candidates to practice medicine in all its branches. An order denying this petition was entered, and Dr. Schleifer appealed. The appeal was allowed on the ground that the ruling of the department was not "fair, reasonable and impartial" — (*Schleifer v. Department of Registration and Education*, N. E. [2d] 398, Appellate Court of Illinois, First Dist., May 29, 1945).

MISCELLANY

DINNER IN HONOR OF DR. MINOT

Dr. George Richards Minot, Nobel Laureate in Physiology and Medicine 1934, professor of medicine, Harvard Medical School and director of the Thorndike Memorial Laboratory of the Boston City Hospital, reached his sixtieth birthday on December 2. A testimonial dinner was tendered him in the Aesculapian Room of the Harvard Club of Boston on December 5 by some of his intimate associates and scientific colleagues. Dr. William B. Castle served as toastmaster, and the speakers included Drs. Henry A. Christian, C. Sidney Burwell, James W. Manary, Laurence B. Ellis, Elliott P. Joslin, Reginald Fitz, J. H. Means and Francis M. Rackemann. The speakers reviewed some of the outstanding personal characteristics and scientific contributions of the guest of honor. Dr. Reginald Fitz, representing the president and House of Delegates of the American Medical Association, took the occasion to award to Dr. Minot its Distinguished Service Medal for his outstanding achievements. Dr. Castle presented to Dr. Minot a bound volume of letters of greeting from numerous scientists throughout the world who have made notable contributions to hematology and nutrition.

COLONEL PARSONS AWARDED LEGION OF MERIT

Lieutenant Colonel C. Langdon Parsons, M.C., A.U.S., on leave of absence as a member of the Surgical Staff of the Massachusetts General Hospital and as assistant in surgery at the Harvard Medical School, was recently awarded the Legion of Merit for meritorious service as chief of the surgical service of a station hospital that handled the majority of cases of maxillofacial injury in the Mediterranean theater from April 1, 1944, to April 1, 1945.

NOTICES

ANNOUNCEMENTS

Dr. William Dameshek announces the removal of his office to 192 Beacon Street, Boston.

Dr. Karl D. Kasparian announces the opening of his office at 395 Commonwealth Avenue, Boston, for the practice of general surgery.

Dr. Leo Maletz announces the opening of his office at 80 Nahant Street, Lynn, for the practice of psychiatry and neurology.

Dr. Joseph D. Wassersug, formerly of the Norfolk County Hospital, announces the opening of his office at 1159 Hancock Street, Quincy, for the practice of internal medicine.

BOSTON SOCIETY OF BIOLOGISTS

A meeting of the Boston Society of Biologists will be held in the Surgical Amphitheater (3A) of the White Building,

Massachusetts General Hospital, on Wednesday, December 19, at 8 p.m.

PROGRAM

Naphthoquinone Antimalarials Dr. Louis F. Fieser
A Fibrous Modification of Insulin Dr. David Waugh
Streptomycin Dr. Donald C. Anderson
Sulfathiadiazole Drs. Manson Meads and Maxwell Finland

HEALTH EDUCATION INSTITUTE

An Institute in Health Education, sponsored by the Massachusetts Tuberculosis League, is to be held at Simmons College, Boston, from February 4 through March 29. The first five weeks of this institute will be devoted to lectures and discussions by local and national experts, and the remaining three weeks to supervised field work.

The primary purpose of the course is to train assistants in health education to work under supervision in the tuberculosis associations of Massachusetts. The training program, however, will also be open to any educational workers in the tuberculosis field desiring a brush-up course. Health workers in other voluntary agencies and in the official agencies of Massachusetts are also invited to attend all or part of the Institute.

Inquiries regarding the detailed program and enrollment in the Institute should be addressed to the Massachusetts Tuberculosis League, 1148 Little Building, Boston 16.

CUTTER LECTURE

The Cutter Lecture on Preventive Medicine will be given by Dr. Donald Hunter, F.R.C.P., physician to the London Hospital, London, England, at 5 p.m. on Monday, December 17, in the amphitheater of Building D of the Harvard Medical School. His subject will be "Research in Industrial Medicine in Great Britain at War."

The medical profession, medical and public-health students, the press and others interested are cordially invited to attend.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, DECEMBER 20

FRIDAY, DECEMBER 21

- *9:00-10:00 a.m. The Clinical Evaluation of an Anti-Hemophilic Fraction of Plasma Dr. Louis K. Diamond Joseph H. Pratt Diagnostic Hospital
- *9:00-10:00 a.m. Medical clinic. Isolation Amphitheater Children's Hospital
- *10:00 a.m.-12:00 m. Medical staff rounds Peter Bent Brigham Hospital
- 10:50 a.m. Squamous Eruptions Dr. George Schwartz. (Post graduate clinic in dermatology and syphilology) Amphitheater Dowling Building Boston City Hospital

MONDAY, DECEMBER 24

- *12:00 m.-1:00 p.m. Clinicopathological conference Peter Bent Brigham Hospital

WEDNESDAY, DECEMBER 26

- *12:00 m. Clinicopathological conference Children's Hospital

*Open to the medical profession

DECEMBER 17 Cutter Lecture. Notice above

DECEMBER 18 South End Medical Club Page 710 issue of December 6

DECEMBER 19 Boston Society of Biologists Notice above

JANUARY 7-APRIL 22 1946 Metropolitan State Hospital Eleventh postgraduate seminar in neurology and psychiatry Page 314 issue of September 6

JANUARY 10 Fatigue Its Significance and Treatment Dr. Frank N. Allan Pentucket Association of Physicians 8:30 p.m. Haverhill

FEBRUARY 2 American Board of Obstetrics and Gynecology Page 514, issue of October 25

FEBRUARY 4-MARCH 29 Health Education Institute. Notice above

DISTRICT MEDICAL SOCIETY

WORCESTER

- JANUARY 9 St. Vincent Hospital
- FEBRUARY 13 Worcester State Hospital
- MARCH 13 Worcester Memorial Hospital
- APRIL 10 Hahnemann Hospital
- MAY 8 Annual meeting

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The pneumonia patients were treated for three or four days; the patients with bronchiectasis or lung abscess, for seven days prior to surgery or for six weeks for purely medical therapy, and those with infective bronchial asthma, for three to ten days.

RESULTS

*Penicillin Blood Levels**

Blood levels for penicillin were obtained in many of the patients and in a series of 6 controls (Tables 1 and 2). Urine levels were not obtained owing to technical difficulties.

Absorption of penicillin from the pulmonary tree into the blood stream was demonstrated by the

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PATIENT'S NAME	DIAGNOSIS	DATE	PENICILLIN BLOOD LEVEL	
			TIME AFTER TREATMENT	LEVEL
				units/cc
M. D.	Infective bronchial asthma	4/27/45 and 4/ 0/45	0 min	0.028
			1 hr	0.028
			2 hr	0.000
T. H.	Chronic bronchitis pulmonary fibrosis possible bronchial asthma	5/ 1/45	0 min	0.000
			1 hr	0.000
			2 hr	0.000
O. M. (Case 1)	Pneumonia of left lower lobe (Type 14)	12/ 0/44	Immediately	0.055
			20 min	0.055
			45 min	0.110
			1 hr 45 min	0.055
E. R. (Case 2)	Pneumonia of left lower lobe (Type 12)	12/30/44	15 min	0.055
			5 min	0.028
			55 min	0.055
			2 hr	0.000
A. P. (Case 3)	Pneumonia of left lower lobe (Type 33)	5/16/45	30 min	0.055
			1 hr	0.028
			2 hr	0.000
M. F. (Case 4)	Pneumonia of left lower lobe (Type 1)	5/18/45	30 min	0.055
			1 hr	0.028
			2 hr	0.028
V. R. (Case 5)	Pneumonia of right upper lobe (Type 1)	5/17/45	0 min	0.000
			1 hr	0.000
			2 hr	0.000
M. G. (Case 6)	Pneumonitis of left lower lobe infarct atelectasis	5, 5/45	30 min	0.028
			1 hr	0.000
			2 hr	0.000
G. R.	Bronchiectasis (left lower lobe)	4/ 4/45	30 min	0.028
			2 hr	0.000
			2 hr	0.000
C. V.	Chronic bronchitis bronchiectasis bronchopneumonia	8/ 8/45	30 min	0.028
			1 hr	0.020
			2 hr	0.000
M. R.	Chronic bronchitis bronchiectasis	8/21/45	0 min	0.055
			1 hr	0.028
			2 hr	0.028
J. G. (Case 8)	Lung abscess (right upper lobe)	5/31/45	1 hr	0.028
W. McD. (Case 9)	Lung abscess (left upper lobe)	4/17/45	0 min	0.220
			1 hr	0.220
			2 hr	0.110
		4/21/45	0 min	0.110
			1 hr	0.110
			1 hr 10 min	0.000
			1 hr	0.000
		5/10/45	3 hr	0.000

repeated during the course of the illness and prior to discharge. No systemic toxic or allergic manifestations were observed. Some patients at first objected to the smell and taste of the penicillin aerosol or found it irritating to the oropharynx. The nurse generally placed the penicillin saline solution in the nebulizer and turned the oxygen regulator on to a flow of 5 to 7 liters per minute. Many of the patients managed the entire treatment themselves.

effective penicillin blood levels, which ranged from 0.028 to 0.223 units per cubic centimeter. Many of the controls, who were free of lung disease, gave zero levels. Generally speaking, higher blood levels were obtained in those with extensive lung involvement of a pyogenic type—that is, those with pneumonia or lung abscess. A single striking ex-

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with nonsurgical bronchiectasis. He employed the technic previously described by Barach and his associates. Olsen used the conventional Vaponefrin nebulizer and 2500 units of penicillin per cubic centimeter of solution, alternating a ten-minute period of nebulization with a ten-minute period of rest. Treatment was extended through a ten-hour day, with an average of 75,000 units of penicillin a day. He observed a greater reduction in the amount of sputum by nebulization than by the parenteral

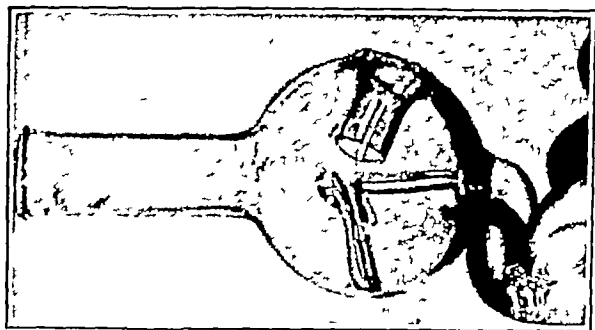


FIGURE 1 Conventional Vaponefrin Nebulizer

This is capable of producing sprays with a particulate size of less than one micron.

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FIGURE 2 Nebulizer in Use

The nebulizer has been enlarged to one-liter capacity by a rubber bag on top; there is a Y-tube attachment to the oxygen regulator.

the best method to prevent the complications that follow pulmonary resection for suppurative disease.

EQUIPMENT AND TECHNIC

The present report is a preliminary study of the use of aerosolized penicillin solutions in the treatment of patients with pneumonia, bronchiectasis, lung abscess and infective bronchial asthma. In our

earliest observations we used the conventional Vaponefrin nebulizer which produced a fine, voluminous mist or smoke screen with a particulate size of 1 micron or less and capable of penetrating the alveoli. A piece of rubber tubing connected the nebulizer with a regulator attached to an oxygen tank. Oxygen flows of 5 to 7 liters were generally sufficient to aerosolize 1 cc of the penicillin solution in approximately fifteen minutes. With this technic large amounts of penicillin aerosol escaped during expiration through the top of the carburetor opening. Following suggestions by Barach, the capacity of the Vaponefrin nebulizer (Figs 1-3) was enlarged to 1 liter to permit condensation and utilization of the expired penicillin. In some cases rebreathing was provided for by the addition of rubber-collecting bags in different positions. To avoid loss of the drug in expiration, a glass Y-tube was placed just proximal to the inlet of the nebulizer. The patient or nurse was instructed to close the open end with one finger

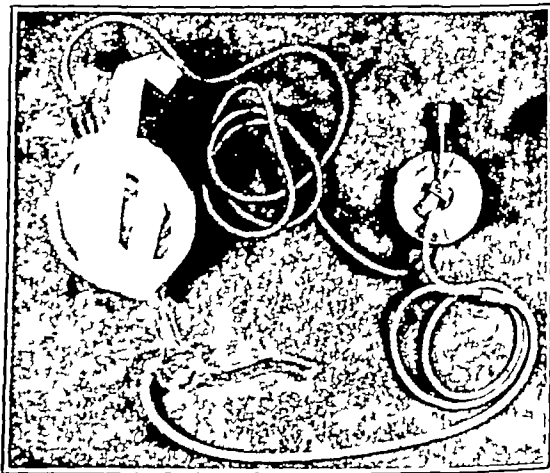


FIGURE 3 Closed Rebreathing Arrangement, with an Emerson Demand Valve for Attachment to the Oxygen Regulator. *This supplies penicillin aerosol on inspiration only and is most suitable for the sickest patients.*

on inspiration and to remove the finger on expiration. With this technic the oxygen bypassed the nebulizer in the expiratory phase of respiration and no penicillin was lost through the top of the nebulizer. Occasionally an Emerson demand-valve system was attached. This had the advantage of automaticity and did not require the patient's or nurse's co-operation with the Y tube. This was of particular value in the seriously ill patients. Commercial sodium penicillin was used in doses of 15,000 to 30,000 units per cubic centimeter of saline solution given at two-hour or three-hour intervals for three days or longer, depending on the nature of the illness. In the patients with bronchiectasis and lung abscess, postural drainage was performed before each treatment with aerosol. We are continuing to modify the apparatus and the technic of penicillin aerosolization.

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O. M. (Case 1)	Pneumonia of left lower lobe (Type 14)	12/30/44	Immediately 20 min 45 min 1 hr 45 min	0.055 0.055 0.110 0.055
E. R. (Case 2)	Pneumonia of left lower lobe (Type 12)	12/30/44	15 min 35 min 55 min 2 hr	0.055 0.028 0.055 0.000
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		5/ 3/45	1 hr	0.000
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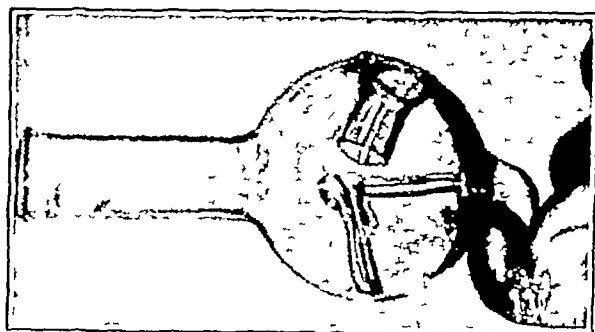


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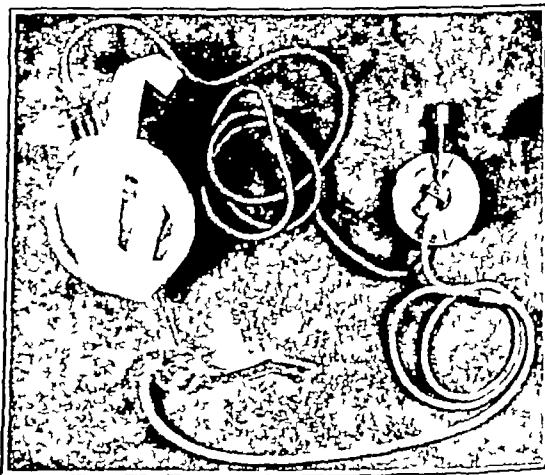


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six to ten days of hospitalization Brief abstracts of these cases follow

CASE 1 O M, a 34-year-old housewife, entered the hospital because of the sudden onset of shaking chills and fever 14 hours previously Following this, she developed precordial pain and cough On admission another chill occurred Physical examination on admission revealed an acutely ill woman breathing with grunting respirations The only other positive findings were in the chest, where at the left base the breath sounds were decreased and a few rales were heard The white-cell count was 20,000, with 90 per cent neutrophils and 10 per cent lymphocytes X-ray examination of the chest revealed faint cloudiness at the left base The sputum on direct Neufeld examination was found to contain a Type 14 pneumococcus The patient was given symptomatic treatment and started on penicillin by inhalation — 20,000 units every 2 hours for nineteen doses and every 3 hours for sixteen doses, a total of 700,000 units The cough and sputum decreased within 24 hours after the commencement of treatment, and the temperature was normal at the end of 48 hours Although the lungs never showed frank consolidation, the lung fields were clear and the sputum culture was negative at discharge on the 10th hospital day

For the penicillin blood levels, see Table 1

CASE 2 E R, a 26-year-old woman, entered the hospital with a history of gradual onset of a "head cold," sore throat, fever and malaise 1 week previously Twenty-four hours before admission she experienced a severe shaking chill, pain in the left chest and a cough productive of blood-streaked sputum On physical examination, the pharynx was injected and at the left base were found dullness, diminished tactile fremitus and distant bronchial breath sounds The white-cell count was 31,000, with 90 per cent neutrophils and 10 per cent lymphocytes X-ray examination of the chest revealed lobar pneumonia of the left lower lobe On mouse inoculation,

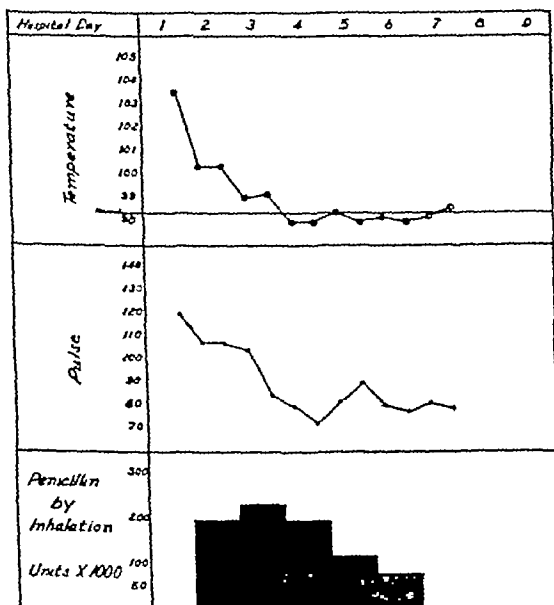


FIGURE 5 Case 2

the sputum was found to contain a Type 12 pneumococcus The patient was given 20,000 units of penicillin by inhalation every 2 hours for twenty-six doses and then every 3 hours for sixteen doses, a total of 840,000 units By the end of the 1st hospital day, the temperature and pulse began to fall On the next day they were still lower and the physical signs were less intense On the 3rd day, a pleural friction rub was heard in the left axilla By the 6th day, the sputum was negative on culture and the lungs were clear The patient was discharged on the 8th day

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CASE 3 A P, a 16-year-old schoolgirl, entered the hospital because of the sudden onset of chilly sensations, fever and pain of a pleuritic nature in the right anterior portion of the chest 12 hours previously Three weeks before admission she had a "cold," with coryza, sore throat and cough Physical examination revealed a toxic, flushed young girl in acute distress At the base of the left lung there was a slight increase in tactile fremitus and also in breath sounds The white-cell count was 14,750, with 90 per cent neutrophils, 76 per cent being mature and 14 per cent band forms, 8 per cent lymphocytes and 2 per cent monocytes X-ray examination showed a typical pneumonia of the left lower lobe Culture of the sputum revealed a Type 33 pneumococcus Adequate hydra-

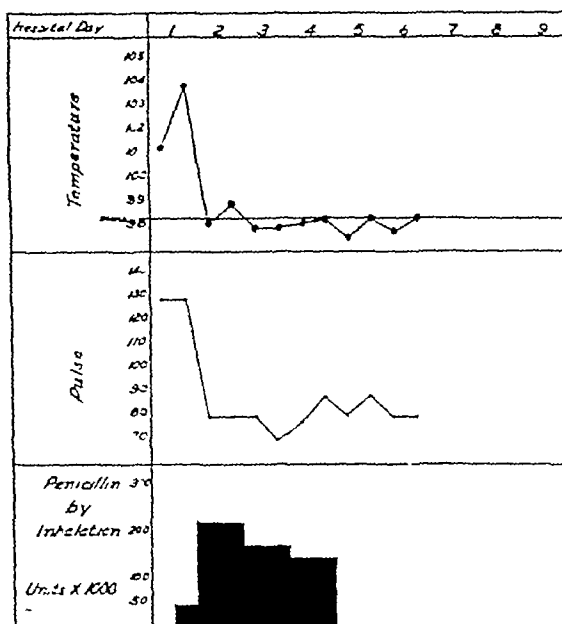


FIGURE 6 Case 3

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CASE 4 M F, a 24-year-old housewife, entered the hospital complaining of a severe "bronchitis" with a heavy cough and sputum for 7 weeks previously Twelve hours previous to admission, she noticed the sudden onset of chills, fever and sharp pain in the left chest and observed that the sputum had become blood-streaked On physical examination, the patient was found to be dyspneic and in obvious distress because of pain, which she attempted to alleviate by splinting the left chest There was diminished expansion, impaired resonance and egophony in the left axilla The white-cell count was 20,600, with 82 per cent neutrophils, 70 per cent being adult and 12 per cent band forms, 14 per cent lymphocytes and 4 per cent monocytes X-ray examination showed pneumonia of the left lower lobe, and culture of the sputum was positive for a Type 1 pneumococcus Penicillin was given by inhalation — 25,000 units every 2 hours for six doses and then every 3 hours for eighteen doses, a total of 600,000 units No frank consolidation ever developed, but on the 3rd day a few coarse rales and wheezes were heard

ception was a patient (Case 5) with Type 1 pneumonia involving two lobes. It was impossible on two occasions to obtain a penicillin blood level, but the clinical response was nevertheless most striking,

Bacterial Pneumonia

A course of penicillin aerosol lasting for three seven days was given to 5 patients with bacterial pneumonia and to 1 patient with pulmonary

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		5/ 9/45	30 min	0.055
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		5/16/45	30 min	0.028
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			2 hr	0.000
M S S	No disease	5/ 9/45	30 min	0.000
			1 hr	0.000
			2 hr	0.000
		5/11/45	30 min	0.000
			1 hr	0.000
			1 hr, 45 min	0.000
		5/18/45	30 min	0.028
			1 hr	0.000
			2 hr	0.000
M B	Cardiac decompensation	6/ 5/45	30 min	0.000
			1 hr	0.000
			2 hr	0.000
A P	Cardiac decompensation, bronchopneumonia	6/ 5/45	30 min	0.028
			1 hr	0.028
			2 hr	0.028
W W	Acute sinusitis	6/ 7/45	30 min	0.000
			1 hr	0.000
			2 hr	0.000
D L.	Pernicious anemia	6/ 7/45	30 min	0.000
			1 hr	0.000
			2 hr	0.000

and there can be no question of the topical effectiveness of the treatment in this case.

We believe that the absorption of penicillin into the blood is not necessarily a measure of the topical effectiveness of penicillin aerosol. The blood levels vary according to the subject's breathing pattern, the equipment used, the dosage and type of penicillin used, the variations of absorption of accumulated pus and secretions and the technic for determining the penicillin levels. Obtaining blood levels is more of academic interest than of practical value. The clinical course is sufficient proof of the topical effectiveness of penicillin aerosol, as is best demonstrated in the patients with pneumonia.

Infective Bronchial Asthma

A course of penicillin aerosol lasting for three to nine days was given to 6 patients with severe chronic infective bronchial asthma. The penicillin-susceptible organisms promptly disappeared and in most cases remained absent during hospitalization. The course of the underlying bronchospasm was not strikingly influenced, and measures employing the principles of repeated bronchiolar relaxation were more effective for its relief. Allergic reactions to penicillin aerosol have been reported,^{29, 31} but were not observed in any of our patients. The possibility of further sensitization in patients with allergic vasomotor rhinitis and bronchial asthma must be appreciated.

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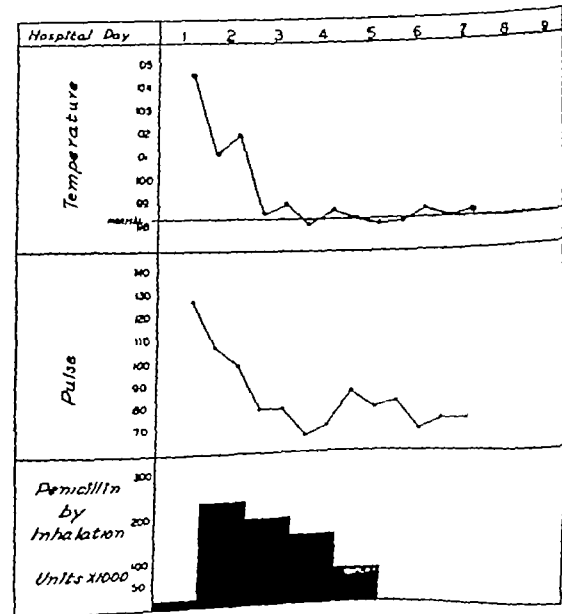


FIGURE 4 Case 1

treatment, and no complications were encountered. The sputum became negative on the second or third day and remained so at the time of discharge, after

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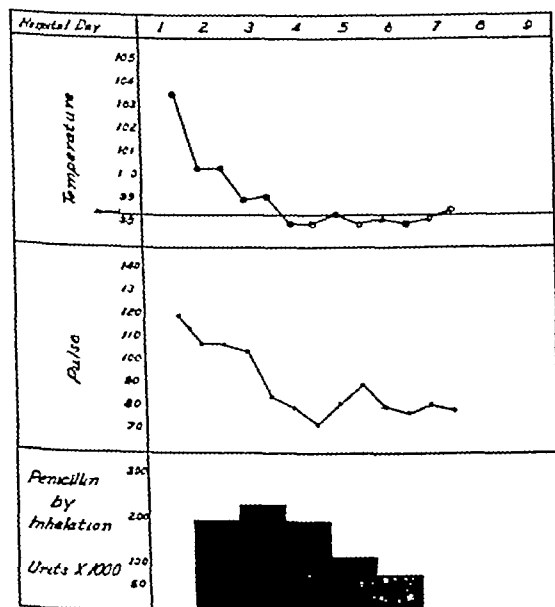


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the sputum was found to contain a Type 12 pneumococcus The patient was given 20,000 units of penicillin by inhalation every 2 hours for twenty-six doses and then every 3 hours for sixteen doses, a total of 840,000 units By the end of the 1st hospital day, the temperature and pulse began to fall On the next day they were still lower and the physical signs were less intense On the 3rd day, a pleural friction rub was heard in the left axilla By the 6th day, the sputum was negative on culture and the lungs were clear The patient was discharged on the 8th day

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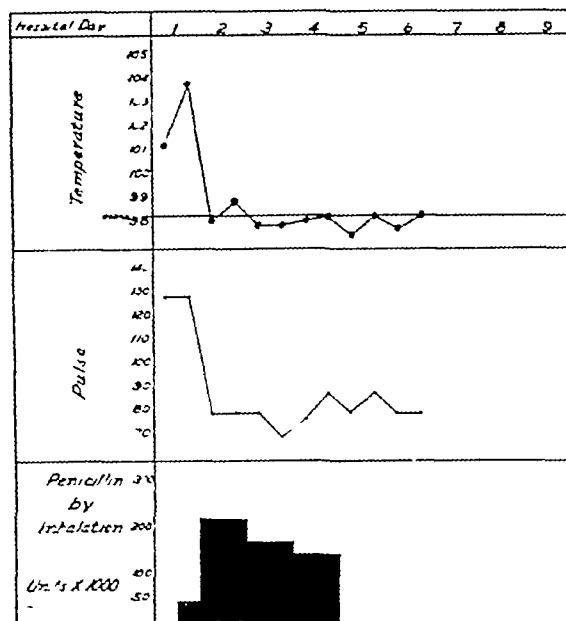


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			1 hr	0.000
			2 hr	0.000

and there can be no question of the topical effectiveness of the treatment in this case.

We believe that the absorption of penicillin into the blood is not necessarily a measure of the topical effectiveness of penicillin aerosol. The blood levels vary according to the subject's breathing pattern, the equipment used, the dosage and type of penicillin used, the variations of absorption of accumulated pus and secretions and the technic for determining the penicillin levels. Obtaining blood levels is more of academic interest than of practical value. The clinical course is sufficient proof of the topical effectiveness of penicillin aerosol, as is best demonstrated in the patients with pneumonia.

Infective Bronchial Asthma

A course of penicillin aerosol lasting for three to nine days was given to 6 patients with severe chronic infective bronchial asthma. The penicillin-susceptible organisms promptly disappeared and in most cases remained absent during hospitalization. The course of the underlying bronchospasm was not strikingly influenced, and measures employing the principles of repeated bronchiolar relaxation were more effective for its relief. Allergic reactions to penicillin aerosol have been reported,^{29, 31} but were not observed in any of our patients. The possibility of further sensitization in patients with allergic vasomotor rhinitis and bronchial asthma must be appreciated.

fraction and pneumonitis. The response was burning. In most cases the clinical charts returned to normal promptly, the patient felt well throughout



FIGURE 4 Case 1

treatment, and no complications were encountered. The sputum became negative on the second or third day and remained so at the time of discharge, after

nisms in the bronchial mucosa and alveoli. This is consistently demonstrated in the pneumonia patients. Absorption of penicillin from the pulmonary tree into the blood stream was demonstrated by the effective blood levels which ranged from 0.028 to 0.055 units per cubic centimeter. In recent report by Meads, Harris and Finland,³³ the minimum inhibiting concentration of penicillin was 0.16 units per cubic centimeter for twenty-seven pneumococcal strains and 0.032 units for nine pneumococcal strains. Levels of 0.032 units inhibited the growth of all but two strains of pneumococcus. Garach and his associates³¹ have pointed out, however, that the absorption of penicillin into the blood and its recovery from the urine are not necessarily measures of the effectiveness of penicillin aerosol. We have come to the same conclusion, and this is strikingly illustrated by the course of the disease in Case 5, which has already been referred to.

We do not advocate the general use of penicillin aerosol for the treatment of pneumococcal pneumonia. The sulfonamides and more recently oral and parenteral penicillin have proved most effective and easier to administer. Purulent complications did not develop in a series of 54 severe cases of pneumococcal pneumonias reported by Meads, Harris and Finland.³³ On the other hand, they attributed the failure of some established purulent complications to clear following parenteral penicillin to its inability to penetrate the infected foci in adequate amounts. Penicillin aerosol may prevent or improve such complications by its topical effectiveness. We are continuing our studies in this direction and hope to find more patients with streptococcal or staphylococcal pneumonia for these are the ones who can be specifically helped.

Bronchiectasis

A course of penicillin aerosol lasting for one to six weeks was given to 5 patients with bronchiectasis. Immediate defervescence, lessening of toxicity, diminution in the amount of daily sputum, loss of foul character of the sputum and rapid disappearance of penicillin-susceptible organisms were observed in all these patients.

Oral or parenteral treatment of patients with bronchiectasis and lung abscess with sulfonamides has been of little value. The bronchoscopic instillation of sulfonamides and aerosolized solutions of sulfonamides in pulmonary suppurative disease has proved more effective.

The value of parenteral penicillin in suppurative pulmonary disease has been largely limited to the prevention of systemic infections. Stookey and his associates³⁴ observed little or no improvement in patients with true bronchiectasis, but noted improvement in 20 per cent of a group of patients with chronic bronchitis. Cough and morning sputum disappeared after the fourth day of treatment in the favorable cases, but in most cases the volume of

sputum was not reduced. Colonies of hemolytic streptococci and staphylococci in sputums were decreased. White and his associates³⁵ on the other hand, demonstrated the value of preoperative and postoperative intramuscular penicillin in a series of 21 cases of pulmonary suppuration. Penicillin was given for one week before operation and for two weeks after it. There were no complicating empyemas. In a series of 20 cases no penicillin was given, and empyema developed postoperatively in 12. These observations further stimulated our interest in penicillin aerosol.

The anatomic changes accompanying bronchiectasis are permanent ones and probably cannot be changed by any therapy save resection. Such patients are subject to repeated episodes of infection, pneumonitis or involvement of other lobes. The mucosal secretions in bronchiectasis largely result from the structural changes in the endothelial lining of the smaller bronchioles. Invasive organisms contribute by further destruction of these bronchioles. Infection can be reduced or eliminated by penicillin aerosol. It thus becomes the ideal therapy for preoperative and postoperative bronchiectasis. The foul sputum can generally be eradicated. The secretions become thinner and less copious, the troublesome cough disappears and the patient's general condition at operation is remarkably better. Postoperatively the penicillin can be given intramuscularly if the patient is too sick for aerosol therapy. From our observations in 2 cases of surgical bronchiectasis, we suggest a course of one to three weeks preoperatively and one week postoperatively, employing the technic described above.

The question arises concerning what can be done for patients with bronchiectasis who refuse surgery and for those for whom resection is not advisable. These make up a large group, with involvement of one or more lobes. Our own observations are too limited for any conclusions but a certain pattern presents itself.

Three patients had bronchiectasis of the left lower lobe, proved by lipiodol bronchograms, two had had their disease for over five years and the third for one year. The 2 former patients had had recurrent episodes of pneumonitis, necessitating repeated hospitalization. Both received a seven-day course of penicillin aerosol, with complete subsidence of symptoms and disappearance of organisms. They have remained relatively free of all symptoms and have been able to work without loss of time for nine and twelve months, respectively. Previously they had received therapeutic and prophylactic sulfonamides, with only short-lasting effect. These are the longest periods of freedom from symptoms and recurrence of pneumonitis that they have been able to enjoy. Unfortunately, they refused recheck lipiodol bronchograms, which would have been of considerable interest. The third patient, a twenty-six-year-old man, had been discharged from military

in the left axilla. The temperature reached normal within 8 hours after the beginning of treatment, and remained there

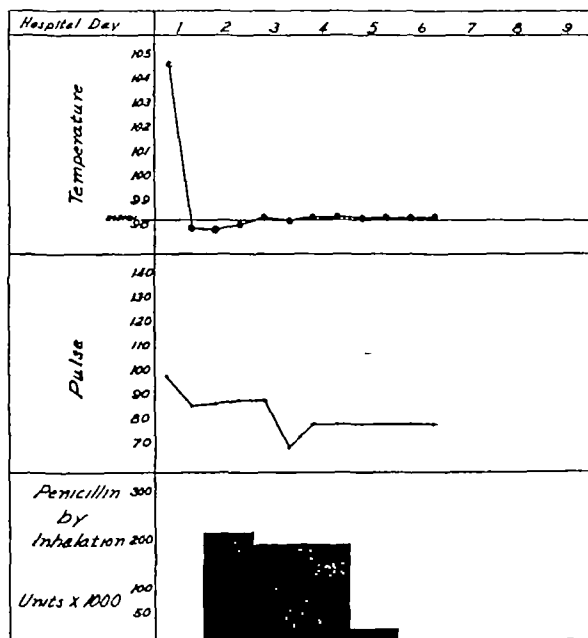


FIGURE 7 Case 4

for the rest of the hospital stay. The sputum was negative on the 3rd day, and the lung fields were clear on the 5th day. For the penicillin blood levels see Table 1.

CASE 5 V R, a 39-year-old man, entered the hospital because of the acute onset of dry cough and vomiting 4 days previously. On the day of admission, the cough became productive and he complained of feverishness and epigastric pain. His physician had given him approximately 5 gm of

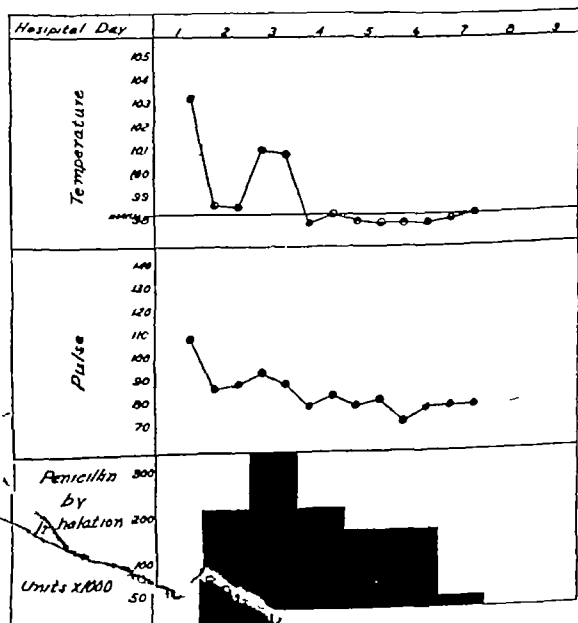


FIGURE 8 Case 5

some sulfonamide, but showing no improvement under this therapy, he entered the hospital. On admission the patient was cyanotic, dyspneic and toxic. Physical examination showed decreased breath sounds and a few moist rales in the right axilla. The white-cell count was 20,250, with 87 per cent neutrophils, 79 per cent being mature and 8 per cent band forms, 12 per cent lymphocytes and 1 per cent basophil.

X-ray examination showed clearing pneumonia of the left lower lobe and pneumonia of the right upper lobe. Culture of the sputum revealed a Type 1 pneumococcus before treatment, was negative for pneumococci 5 hours after the beginning of treatment and showed the growth of no organisms 2 days after the start of treatment. The patient was started on penicillin by inhalation—25,000 units every 2 hours for seven doses, to be followed by 25,000 units every 3 hours. The temperature dropped to normal 8 hours after the commencement of treatment, but rose to 101°F on the 2nd hospital day. It was discovered that technical difficulties had developed, so that the patient received no penicillin for 10 hours. Resumption of the treatment was carried out with 50,000 units every 2 hours for six doses, 25,000 units every 2 hours for five doses and finally 25,000 units every 3 hours for nineteen doses, a total of 1,075,000 units. As soon as treatment was resumed, the temperature dropped to normal and remained there. On the 5th day, the lung fields were clear and the cough and sputum were less.

The penicillin blood level was zero 30 minutes, 1 hour and 2 hours after treatment (Table 1).

CASE 6 M G, a 68-year-old woman, entered the hospital because of the sudden onset of sharp pain in the left chest, aggravated by coughing, deep breathing and motion, 14 hours previously. She later developed a high fever and a slight dry cough. On physical examination, the only positive find

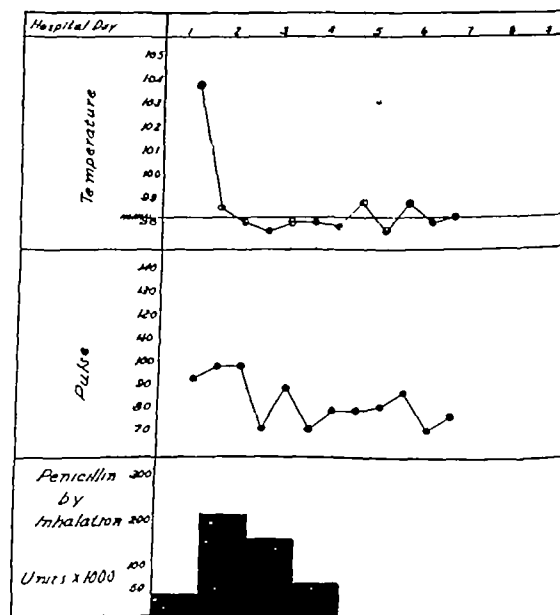


FIGURE 9 Case 6

ings were in the chest, where there was slight dullness, diminished vocal and breath sounds and a few moist rales on deep inspiration in the left chest anteriorly. The white cell count was 26,450, with 92 per cent neutrophils, 87 per cent being mature and 5 per cent band forms, 7 per cent lymphocytes and 1 per cent monocytes. X-ray examination showed pneumonia of the left lower lobe, with plate atelectasis at the left base. No pneumococci were ever recovered from the sputum or throat cultures. The patient was started on inhalation of penicillin—25,000 units every 2 hours for six doses and then every 3 hours for fifteen doses, a total of 525,000 units. The temperature dropped dramatically from 104 to 99°F by the end of the 1st hospital day. Pleuritic pain continued for several days. The lung fields were clear on the 10th hospital day.

For the penicillin blood levels, see Table 1.

These cases of bacterial pneumonia are, it is believed, the first to be treated with penicillin aerosol. At the outset it was hoped to show the topical bacterial effectiveness of penicillin aerosol on the or-

was started on intramuscular penicillin, 15,000 units every 3 hours, and on penicillin aerosol, 25,000 units every 3 hours. The intramuscular penicillin was gradually reduced, but the penicillin aerosol was continued in full doses. Within 1 week x-ray films showed marked improvement in the lung disease, and after 16 days penicillin aerosol was discontinued. Shortly thereafter x-ray films showed normal lung fields and the patient was much improved. She was discharged after 3 months of hospitalization to convalesce from her fractures.

From our observations it appears that penicillin aerosol should be employed in all cases of multiple

type, penicillin aerosol is likely to prove of no curative value but is of possible preoperative benefit. In the nonodoriferous, aerobic type, our experience with the single case described was most unusual. It appears to be a physiologically sound conclusion that the postpneumonic, aerobic, non-odoriferous lung abscess may best lend itself anatomically to topical aerosol therapy, in contrast to the odoriferous type. It may be possible to avoid

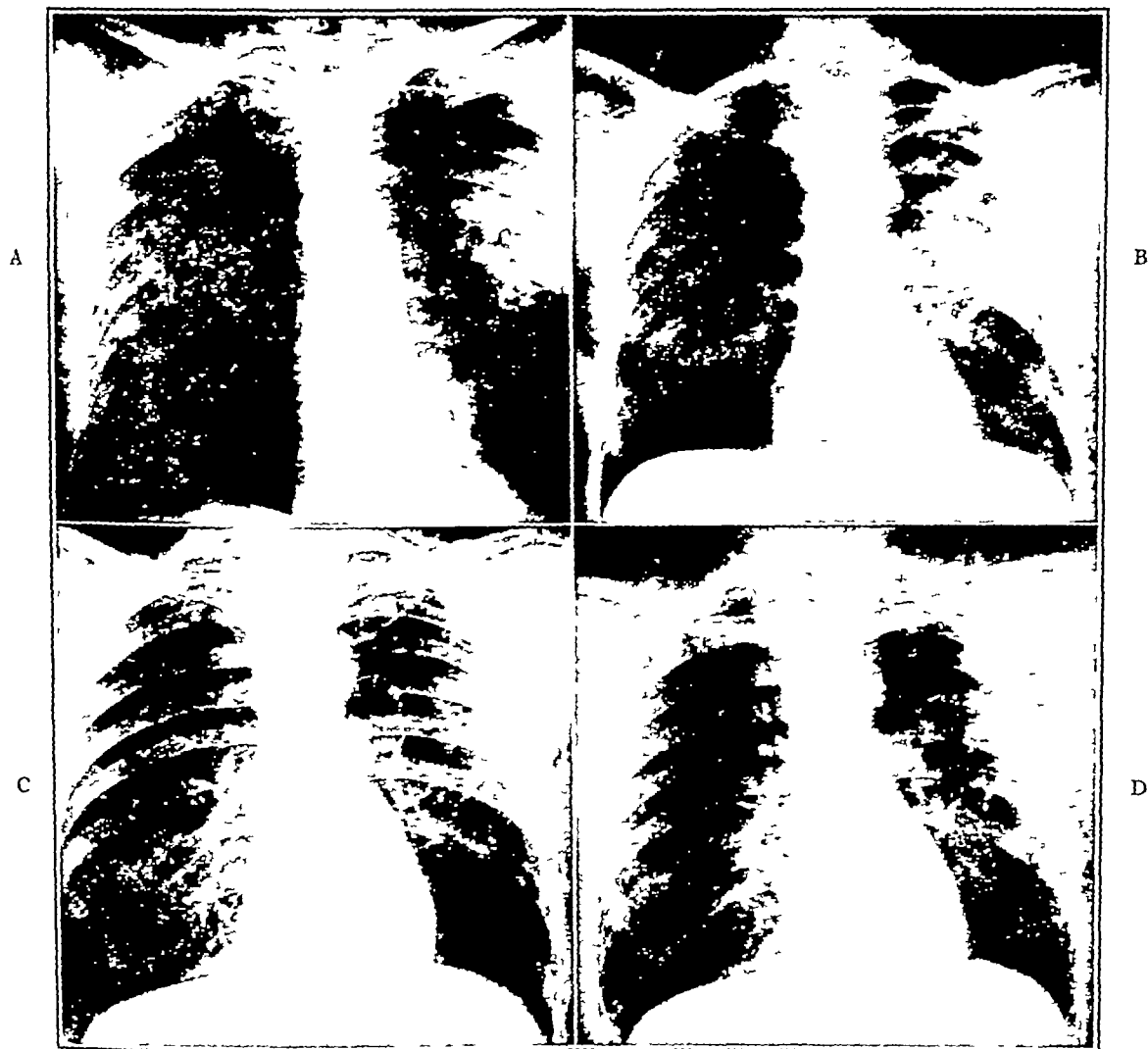


FIGURE 10 Roentgenogram of Chest in Case 9

A—This film was taken on admission, there is a lemon-sized lung abscess in the left upper lobe, with irregular cavitation, a fluid level and pneumonia. B—This film was taken after five days of penicillin aerosol therapy, there is an increased area of density in the midouter zone. C—This film was taken after one month of aerosol therapy, there is evidence of pneumonia and fibrosis in the left upper lobe, but no fluid level. D—This film was taken two months after stopping aerosol therapy, the patient was symptom free and had gained 25 pounds in weight, recovery being considered complete.

lung abscess for courses as long as four to ten weeks. After a suitable rest period another course may be given if necessary. In patients with acute or chronic lung abscess of the odoriferous, anaerobic

surgery in these cases with an effective program of penicillin aerosol. In most cases we have not employed intramuscular penicillin along with penicillin aerosol.

service because of bronchiectasis of the left lower lobe, acquired following exposure and severe respiratory infections. He also had pansinusitis with polyposis. He was given a seven-day course of penicillin aerosol, soon became symptom-free and subsequently received the proper surgical care for the polyps. A repeat lipiodol bronchogram again revealed bronchiectasis in the left lower lobe. The patient has remained symptom-free and has been able to perform his regular work for the last four months. Another and longer course of penicillin aerosol, directed nasally as well as to the lungs, will be given six months after the first course.

These 3 patients are most pleased with the results thus far obtained. Their vital capacities have increased from 30 to 40 per cent above the pre-aerosol level and have remained fairly constant at the improved figure. Each patient has been urged to have a lobectomy performed and has refused. All three have been advised that they will ultimately probably require lobectomy and that penicillin aerosol may serve temporarily by sterilizing the "stagnant cesspool."

No untoward results of penicillin aerosol have been seen. Many patients with bronchiectasis probably require repeat courses at three-month or six-month intervals. Penicillin is now within everyone's reach, and the therapy can be easily carried out in the patient's home. The more resistive cases will undoubtedly require therapeutic courses up to six weeks or longer. Those with sinus involvement will require penicillin aerosol by the nasal route and possibly subsequent sinus surgery. Studies along this line are being made for a subsequent report.

Lung Abscess

A course of penicillin aerosol was given to 4 patients with lung abscess. Reports of these cases follow.

CASE 7 L S, a 38-year-old man, developed an acute, fulminating, putrid lung abscess with cavitation following tonsillectomy. He was desperately ill on admission, with a temperature of 104°F. A chest plate revealed a large lung abscess with a cavity measuring 8 by 8 cm, together with a fluid level. There was a hacking cough productive of foul, dark sputum containing lung tissue. Sputum culture revealed Friedländer's organisms, streptococci, staphylococci, fusiform organisms and many others. The patient was given a 4-day course of penicillin aerosol, without any clinical improvement except in the foul odor of the sputum and breath. Following a rib resection and drainage on the 5th hospital day, he expired suddenly 4 hours postoperatively.

CASE 8 J G, a 50-year-old man, was admitted complaining of a cough productive of foul sputum of 1 year's duration. He had been operated on 5 years previously for an abscess in the right upper lobe. The sputum on admission was yellowish, thick and foul-smelling. Culture revealed an alpha-hemolytic streptococcus, diphtheroids and *Neisseria flavis*. Chest plates showed an extensive abscess in the right upper lobe, with bronchiectasis. During a seven-day course of penicillin aerosol, the sputum became less productive and more watery. A sputum culture at the end of therapy revealed no streptococci, although the diphtheroids and *N. flavis* survived. The foul odor of the sputum soon disappeared, the patient felt better, and the appetite improved. A right pneumo-

nectomy was performed on the 8th day, no growth was obtained from the chest fluid postoperatively. During convalescence penicillin was given intramuscularly and the patient made an uneventful recovery.

CASE 9 W McD, a 59-year-old man, entered the hospital with a history of a "head cold" 6 months previously, followed by a cough productive of light-yellow sputum. This was accompanied by fever and chilliness. Two months later he caught another cold, which persisted. This was accompanied by a chronic cough productive of dark-brown and foul-tasting sputum, which interfered with his sleep. The sputum was at first small in amount, but gradually increased up to 500 cc a day, more being raised in the morning than at night. On three occasions there were small hemoptyses. There were anorexia, fatigue and a weight loss of 20 pounds. One week before entry darting sharp pains began through the left shoulder, radiating to the anterior chest and lasting for a few seconds. The nails became slightly clubbed during this illness. A chest plate on admission (Fig. 10) revealed a lemon-sized lung abscess with a fluid level in the left upper lung field and slight mottling about the abscess, due to pneumonic changes. Bronchoscopy revealed no endobronchial tumor. On the 1st hospital day, the patient raised 500 cc. of moderately foul sputum containing alpha hemolytic streptococci, *N. catarrhalis*, diphtheroids and *Haemophilus hemolyticus*. He was placed on bed rest, postural drainage and oral sulfadiazine. Maximum sulfadiazine levels of 9.3 to 14.1 mg per 100 cc were maintained. This program cleared up the low-grade fever but did not otherwise alter the clinical course. On the 10th day, the patient was still raising 500 cc of sputum with the same physical and bacteriologic characteristics of the initial sputum. The chest plate revealed a more definite pneumonitis surrounding the large lung abscess. On the 11th day, a course of penicillin aerosol, 30,000 units per cubic centimeter of saline solution every 3 hours, day and night, was begun. Extremely effective penicillin blood levels were obtained as follows: 30 minutes after aerosol, 0.220 units, 1 hour after aerosol, 0.220 units, 2 hours after aerosol, 0.110 units, and 3 hours after aerosol, 0 units. The patient was very co-operative, and within 4 days the appetite improved and the cough lessened. Within 10 days of the commencement of penicillin aerosol, the sputum was no longer foul-tasting and had decreased from 500 to 250 cc a day. The cough practically disappeared and the appetite was normal. By the 18th day, the patient was raising only about 50 cc of sputum and felt "wonderful." At the end of 42 days of treatment, he had only a slight cough productive of less than 15 cc of sputum daily, and had fully regained his normal strength and weight. Sputum culture shortly after onset of treatment revealed only an atypical Friedländer bacillus and *Escherichia coli*. Serial x-ray studies showed a striking progressive improvement, with resolution and ultimate fibrosis of the entire process. The patient was discharged after 8 weeks of hospitalization, and subsequent clinical and x-ray checkups revealed a complete cure.

CASE 10 L C, a 54-year-old graduate nurse, was struck by an automobile, receiving fractures of the left humerus and the 8th rib on the right. She was hospitalized and the fractures were treated. On the 10th hospital day, signs and symptoms of pneumonia of the right lower lobe appeared and sulfadiazine was begun. Because of a poor response, this treatment was changed to penicillin intramuscularly, 15,000 units every 4 hours. One week later the patient complained of pain in the right leg, and a diagnosis of phlebotrombosis was made. Vein ligation was advised, but was not carried out because of the patient's condition. The pneumonia cleared slowly, but an accumulation of fluid was found in the right chest. This was tapped and 650 cc of reddish-brown fluid was removed. A culture showed no growth. Sulfadiazine and penicillin were again given, and within 1 week x-ray and physical signs showed the lung fields to be clear. On the 39th day, severe precordial pain suddenly began, with sweating, cyanosis, dyspnea and apprehension. Coronary-artery disease was suspected. Following this, similar episodes of chest pain continued, and the possibility of multiple pulmonary infarcts arose. On the 52nd day, following one of these episodes, the temperature again became elevated, and sulfadiazine was resumed. A cough productive of purulent sputum soon developed, and a chest plate revealed an abscess of the left upper lobe. Ten days later the patient

was started on intramuscular penicillin, 15,000 units every 3 hours, and on penicillin aerosol, 25,000 units every 3 hours. The intramuscular penicillin was gradually reduced, but the penicillin aerosol was continued in full doses. Within 1 week x-ray films showed marked improvement in the lung disease and after 16 days penicillin aerosol was discontinued. Shortly thereafter x-ray films showed normal lung fields and the patient was much improved. She was discharged after 3 months of hospitalization to convalesce from her fractures.

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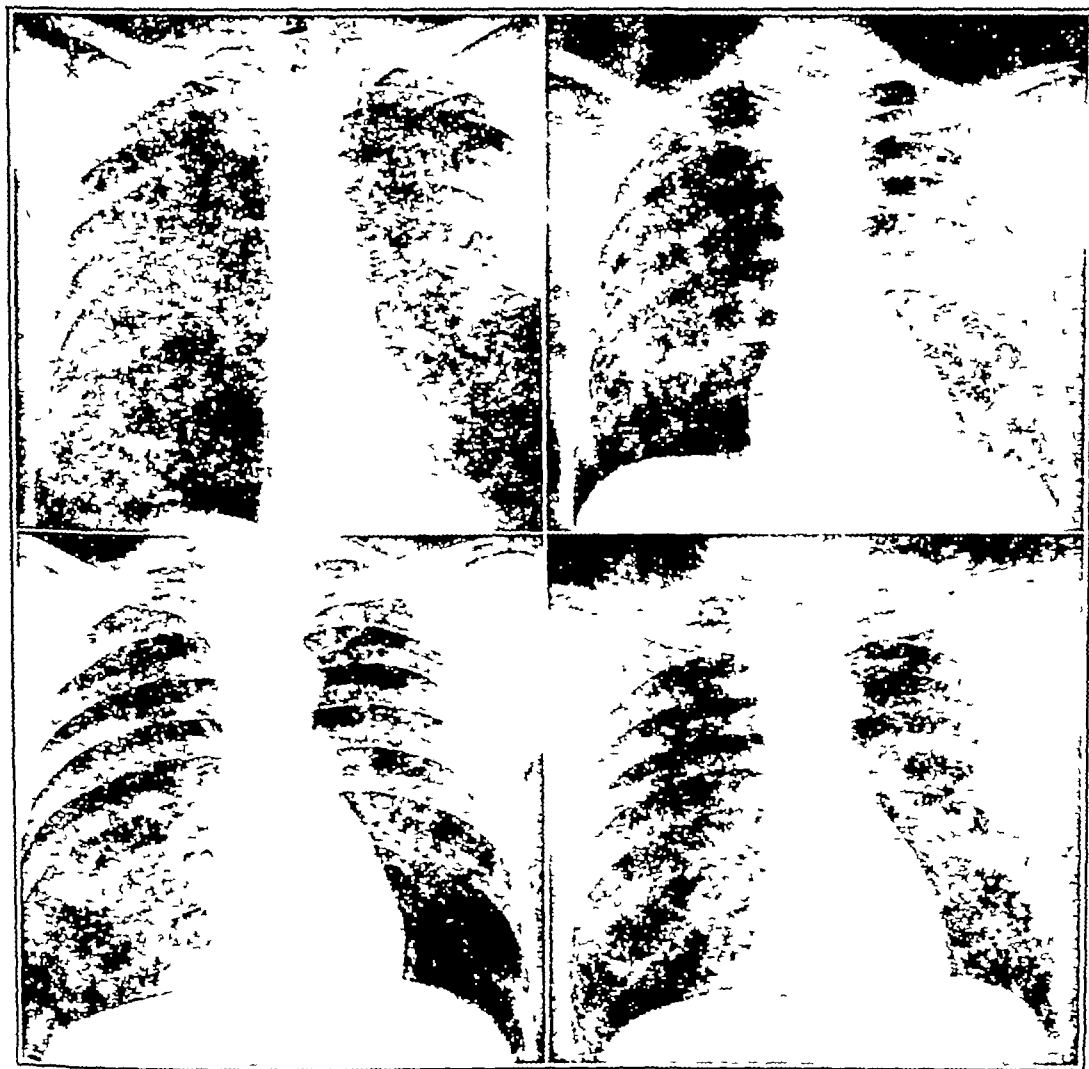


FIGURE 10. Roentgenogram of Chest in Case 9.

A—This film was taken on admission; there is a lemon-sized lung abscess in the left upper lobe with irregular cavitation, a fluid level and pneumonitis. B—This film was taken after five days of penicillin aerosol therapy; there is an increased area of density in the midouter zone. C—This film was taken after one month of aerosol therapy; there is evidence of pneumonitis and fibrosis in the left upper lobe, but no fluid level. D—This film was taken two months after stopping aerosol therapy; the patient was symptom free and had gained 25 pounds in weight, recovery being considered complete.

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surgery in these cases with an effective program of penicillin aerosol. In most cases we have not employed intramuscular penicillin along with penicillin aerosol.

SUMMARY AND CONCLUSIONS

Penicillin aerosolization was employed in 21 patients with serious respiratory disease

The clinical course of 6 patients with infective bronchial asthma was not altered, although the penicillin-susceptible organisms were eradicated

Striking clinical cures were promptly obtained in 5 patients with pneumococcal pneumonia and in 1 patient with an acute pulmonary infarction and pneumonitis. Penicillin blood levels of 0.028 to 0.055 Oxford units per cubic centimeter were obtained in 5 patients. In a patient with Type 1 lobar pneumonia the level was not detectable. Observations in this series definitely proved the bacterial effectiveness of topical penicillin aerosol in pulmonary disease.

Five patients with bronchiectasis were successfully treated, 2 patients before lobectomy and the other 3 entirely medically. Defervescence, lessening of toxicity, diminution in the amount of daily sputum, loss of foul character in the sputum, rapid disappearance of penicillin-susceptible organisms, improvement in appetite and a gain in weight were uniformly observed. Such therapy is believed to be more helpful than sulfonamides or penicillin parenterally.

Four patients with lung abscess were treated with penicillin aerosol. One of them, with a fulminating putrid lung abscess, died on the fifth hospital day following surgery. Another, with a chronic putrid lung abscess, was adequately prepared for an uneventful lobectomy. The third patient, with a large, nonodoriferous, aerobic type of lung abscess, with a fluid level, was entirely cured after six weeks of therapy. The fourth patient, with multiple lung infarcts and a lung abscess, improved slowly but completely. Penicillin aerosolization has a definite value in the treatment of patients with serious respiratory disease. Effective local medication with adequate systemic blood levels for most of the penicillin-susceptible organisms can be obtained. Systemic blood and urine levels, however, are merely an indication of absorption through the lung and are not necessary to prove topical effectiveness. No toxic results were observed in this series. The technical difficulties have been overcome. Procedures for various age groups with different breathing patterns can be arranged. It is hoped that other antibiotic agents, when available and if nontoxic, may prove of some value in the form of an aerosol in similar cases.

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CLINICAL AND LABORATORY STUDIES OF NINETY-ONE WORKERS WITH APICAL SYSTOLIC MURMURS

CAPTAIN IRVING NORMAN WOLFSON, M C, A U S

THE attitude of the medical profession toward systolic murmurs of the heart has been one of great inconsistency. In former years, many physicians thought that the presence of such a murmur was indicative of heart disease. The opposite attitude is expressed in the frequently quoted statement of Mackenzie that the physician would do well to throw away his stethoscope while evaluating cardiac murmurs. In an attempt to investigate the significance of apical systolic murmurs, 91 workers with this lesion were studied clinically, as well as with x-ray films and electrocardiograms. The results are reported below.

The solution of this problem is important today for two reasons. In selecting men for the armed services, it is important to know whether the hearts of persons with systolic murmurs that cause no symptoms of failure in civilian life can continue to function normally under the increased demands of military service. If the systolic murmur is an indication of heart disease, it would be more economical to reject such men at the induction centers rather than to have an appreciable number of them break down after the expenditure of time and money in training. The scope of the problem is shown by the fact that of all men examined for induction, 159 per cent are found to have rheumatic or valvular heart disease and are usually rejected. At the same time, 0.53 per cent have murmurs considered to be functional and are accepted.¹ A survey of 45,000 candidates for air training disclosed the presence of valvular disease in 100.²

Even if the finding of a systolic murmur is not indicative of any potential impairment of cardiac function, another distinct problem arises. There has been an increase in the use of prophylactic measures against subacute bacterial endocarditis in the form of sulfonamide administration before performing minor infective surgical procedures on patients with valvular lesions. One must therefore decide whether patients with systolic murmurs have diseased valves that are more susceptible than are normal valves to infection with the usual causative organisms. If this should be the case, it would be justifiable to use prophylactic sulfonamide medication before removing the teeth or tonsils. Furthermore, if the chemoprophylaxis of rheumatic-fever recurrences by the administration of constant small doses of sulfonamides during the winter months becomes widespread, it will be necessary to decide how many patients with systolic murmurs and negative past histories have actually had subclinical attacks of rheumatic fever that produced the murmur.

REVIEW OF THE LITERATURE

A prominent reason for the present inconsistent attitude toward systolic murmurs is the frequency with which these are encountered in apparently normal subjects. Thus, Thayer³ found that over one third of 218 seemingly healthy persons in the first four decades of life had apical systolic murmurs in the recumbent position. Freeman and Levine⁴ discovered apical and basal systolic murmurs in one fifth of 1000 subjects.

Evidence of the unimportance of systolic murmurs is afforded by Blumenthal,⁵ who followed 100 patients with this lesion for an average period of seven years. During this time, only 4 patients developed other cardiac abnormalities. Contratto⁶ reported on 127 Harvard students with apical or basal systolic murmurs the significance of which was uncertain after initial examinations. After a follow-up lasting two to three years, he was unable to make a diagnosis of organic valvular disease in any case, and several of the patients took part in football and other athletics during their college careers.

Strong evidence that systolic murmurs are of prognostic significance may be obtained from insurance figures quoted by McCrudden.⁷ Having analyzed the independent and concordant findings of three insurance companies, this writer points out that patients with systolic murmurs have a mortality due to heart disease as much as seven to ten times greater than expected. Furthermore, this mortality is increased when the murmur is accompanied by cardiac hypertrophy or a history of rheumatic fever. A separate study revealed that deaths in patients with murmurs considered functional occurred with four times the frequency expected.

White⁸ reported on 1000 patients with apical systolic murmurs, including some with accompanying diastolic murmurs. Although stating that slight apical systolic murmurs are frequent and are in themselves of little or no importance in the absence of other signs of heart trouble, he found that only 19 per cent of the patients had normal hearts and that in 6 per cent normalcy was doubtful. The rest of the patients had organic heart disease. Furthermore, the incidence of organic heart disease increased with the intensity of the systolic murmur, ranging from 56 per cent in patients with slight murmurs to 98 per cent in those with loud ones. Similar findings are reported by Freeman and

SUMMARY AND CONCLUSIONS

Penicillin aerosolization was employed in 21 patients with serious respiratory disease.

The clinical course of 6 patients with infective bronchial asthma was not altered, although the penicillin-susceptible organisms were eradicated.

Striking clinical cures were promptly obtained in 5 patients with pneumococcal pneumonia and in 1 patient with an acute pulmonary infarction and pneumonitis. Penicillin blood levels of 0.028 to 0.055 Oxford units per cubic centimeter were obtained in 5 patients. In a patient with Type 1 lobar pneumonia the level was not detectable. Observations in this series definitely proved the bacterial effectiveness of topical penicillin aerosol in pulmonary disease.

Five patients with bronchiectasis were successfully treated, 2 patients before lobectomy and the other 3 entirely medically. Defervescence, lessening of toxicity, diminution in the amount of daily sputum, loss of foul character in the sputum, rapid disappearance of penicillin-susceptible organisms, improvement in appetite and a gain in weight were uniformly observed. Such therapy is believed to be more helpful than sulfonamides or penicillin parenterally.

Four patients with lung abscess were treated with penicillin aerosol. One of them, with a fulminating putrid lung abscess, died on the fifth hospital day following surgery. Another, with a chronic putrid lung abscess, was adequately prepared for an uneventful lobectomy. The third patient, with a large, nonodoriferous, aerobic type of lung abscess, with a fluid level, was entirely cured after six weeks of therapy. The fourth patient, with multiple lung infarcts and a lung abscess, improved slowly but completely. Penicillin aerosolization has a definite value in the treatment of patients with serious respiratory disease. Effective local medication with adequate systemic blood levels for most of the penicillin-susceptible organisms can be obtained. Systemic blood and urine levels, however, are merely an indication of absorption through the lung and are not necessary to prove topical effectiveness. No toxic results were observed in this series. The technical difficulties have been overcome. Procedures for various age groups with different breathing patterns can be arranged. It is hoped that other antibiotic agents, when available and if nontoxic, may prove of some value in the form of an aerosol in similar cases.

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A murmur was considered to be associated with a cardiovascular abnormality when the patient had a history of rheumatic fever, hypertension, roentgenologic evidence of cardiac enlargement, an abnormal electrocardiogram or other disease that might be expected to produce a murmur

RESULTS

There have been several sources of confusion in the evaluation of systolic murmurs. It seems logical to treat basal and apical murmurs separately, since different lesions may be involved in their production. The intensity of the murmur may also be significant, and this has received attention in the work of White,⁸ and of Freeman and Levine⁴ discussed above. Levy, Stroud and White,¹² reporting on the results of re-examination of men rejected for military duty, also mention that the intensity of the murmur was used as a criterion for acceptability. Third, the age of the patient should receive consideration, in view of the pathological study of Rednick,¹⁰ already discussed, in which the type of valvular lesion was related to the patient's age.

Significance of Intensity

The relevant facts obtained with the methods already described are set forth in Table 1. Forty-seven per cent of the murmurs were classified as faint, 31 per cent as moderate and 22 per cent as loud. It is apparent that 78 per cent of these apical systolic murmurs were associated with at least one cardiovascular abnormality according to the criteria outlined. This proportion was lower

Even if it is assumed that the significance of the murmur increases with intensity, it is apparent that faint systolic murmurs cannot be ignored and that a majority are associated with cardiovascular abnormalities. This has been the conclusion of others who have attempted to evaluate the significance of the intensity of murmurs.^{4, 8} A relevant and vivid example is that of a nineteen-year-old girl who was told that she had had rheumatic fever at the age of 2 and who had an attack of polyarthritis at seventeen. As long as she could remember, she had had almost yearly episodes of heart failure, during which she was confined to bed with cough, ankle edema, dyspnea and orthopnea. A teleroentgenogram disclosed only slight exaggeration of the left middle cardiac segment. The PR interval of the electrocardiogram was 0.26 second, but on auscultation the only remarkable finding was a faint systolic murmur over the fourth interspace, to the left of the sternum.

Significance of Age

When the cases are divided into three age groups (Table 2) and the same factors are analyzed, several significant conclusions may be drawn. In all but 1 of the patients above fifty the apical systolic murmur was significant and was most frequently associated with hypertension. This is in sharp contrast to the lower age groups, in which the murmur was rarely associated with hypertension. In the youngest age group, below twenty-five, a history of rheumatic fever was obtainable in more than half the cases, this history was present less frequently as the age increased, and was found in only one fifth of the patients over fifty. From this it may be concluded that an apical systolic murmur in a young patient

TABLE 1 Significant Clinical and Laboratory Findings Related to the Intensity of the Murmur

FINDING	FAINT		MODERATE		LOUD		TOTAL	
	(43 CASES)		(28 CASES)		(20 CASES)		(91 CASES)	
	No	Per-centage	No	Per-centage	No	Per-centage	No	Per-centage
History of rheumatic infection	14	33	11	39	7	35	32	35
Hypertension	6	14	11	39	5	25	22	24
Roentgenologic enlargement	9	21	11	39	9	45	29	32
Abnormal electrocardiogram	19	44	10	36	9	45	38	42
PR interval greater than 0.20 sec.	9		4		3		16	
Left-axis deviation	3		3		4		10	
ST and T abnormalities*	6		4		2		12	
Low voltage of QRS†	3		2		1		6	
QRS duration of 0.15 sec.	1		0		0		1	
Miscellaneous‡	3		0		1		4	
Total cases with at least one of above positive findings	32	74	22	79	17	85	71	78

*Deviation of ST greater than 1 mm from isoelectric line, T₁ and T₂ inverted or less than 1 mm in amplitude. T₄ inverted or less than 0.5 mm in amplitude.
†Total amplitudes of QRS of limb leads less than 15 mm, with none greater than 5 mm.
‡Includes 1 case each of angina pectoris, hyperthyroidism (pulse rate of 120), leukemia and anemia (red-cell count of 3,500,000).

in the cases in which the murmurs were faintest (74 per cent) and increased proportionately with increased intensity of the murmur, reaching 85 per cent when the murmur was loud. The increase was, however, only slight and may not be significant in view of the small number of cases involved.

is likely to be associated with rheumatic fever, whereas in older persons hypertension is frequently present. Presumably, this is partly due to the failure of rheumatic patients to survive to old age. The higher proportion of abnormal electrocardiograms in the oldest age group is entirely due to the

Levine,⁴ who found that every one of 19 patients with apical and basal murmurs of intermediate intensity had disease that adequately explained the presence of the murmurs, whereas of 196 patients with fainter murmurs 45 had no evidence of disturbed cardiovascular function. The radiographic and electrocardiographic findings in these 45 patients were not, however, mentioned. These authors concluded that many systolic murmurs that are regarded as functional are in fact organic in the sense that there is a structural change in the valves causing the murmur.

Fineberg and Steuer⁹ followed 100 children with loud apical systolic murmurs for six years. Sixty per cent of them still had the murmurs after this period, 30 per cent had developed signs of additional valvular lesions, and in 8 per cent the murmur had disappeared. There were 2 deaths, including one from subacute bacterial endocarditis. The incidence of development of frank valvular disease was higher in the patients with a history of rheumatic fever or chorea, as well as in those with clinical or roentgenologic evidence of enlargement of the heart.

Rednick¹⁰ has attacked the problem from the pathological viewpoint. He studied the autopsy reports of 268 patients with systolic murmurs — including 33 who also had diastolic murmurs — obtained from examining over a thousand consecutive protocols. In only 4 per cent of these cases was there no clinical or pathologic explanation for the murmur. In 18 per cent in which the heart showed no pathologic changes, there was present a clinical explanation for the murmur, such as hypertension, anemia or tachycardia. The remainder of the cases (78 per cent) showed pathologic lesions that could have been responsible for the murmurs. The last group may be divided into two. Forty-four cases (16 per cent of the total) showed evidence of valvular stenosis or insufficiency. One hundred and thirty-six cases (51 per cent) had minor abnormalities, such as sclerotic, thickened or calcified valves, that were not sufficient to cause incompetence. The latter group consisted of persons with an average age of seventy-three years.

MATERIAL AND METHODS

The material for this study was obtained from examinations of civilian workers at a field under the supervision of an air-service command. The murmurs were usually discovered in the course of pre-employment medical examinations and it was my responsibility to evaluate these and to recommend medically correct placement of the worker. A smaller number of the murmurs were heard in the course of examinations conducted for the evaluation of noncardiac defects.

All workers examined were employed on full time, performing light and arduous duties. Thirty-nine had symptoms referable to the cardiorespiratory system. In 21 of these patients, however, excessive

short-windedness was the sole complaint. The ages varied from sixteen to seventy-four years, with an average of thirty-eight. There were 51 men and 40 women.

Only persons with systolic murmurs restricted to or maximal at the apex of the heart are included in this study. The apex is taken to include any point below the fourth rib and to the left of the sternum. If a separate basal murmur was present or if the murmur was louder at the base than at the apex, the case was not included. On the other hand, all apical systolic murmurs are included, even those audible only in certain positions. Systolic murmurs present only after exertion are excluded in view of the extremely high frequency of this finding.⁴ All patients were auscultated in the left lateral recumbent position after exertion and were excluded from the study if a diastolic murmur became audible under these circumstances. In this way it was hoped to ascertain the cardiac status of persons who had systolic murmurs as their main abnormality on physical examination of the heart, since it is this auscultatory finding that is the source of confusion.

Careful inquiries were made for a past history of rheumatic infection, and this was said to be positive only when it included at least one of the following: an illness characterized by swollen, painful, tender joints, an illness of several weeks' duration, diagnosed at the time by the attending physician as rheumatic fever, prolonged bed rest recommended by a physician because of the discovery of a heart murmur, and St. Vitus's dance. A small number of patients had questionable histories, such as fleeting joint pains or a murmur after recovery from scarlet fever. These patients were classified as having no history of rheumatic infection.

Patients were classified as hypertensive if the systolic pressure exceeded 150 mm. or the diastolic 90 mm. All elevated pressures were repeated after the patient was recumbent for five minutes, since it was not practicable to wait for the desired twenty to thirty minutes.

Teleroentgenograms were taken of most of the patients, and almost all the remainder were fluoroscoped. If the latter procedure showed any questionable abnormality, a teleroentgenogram was taken. A heart was classified as enlarged only if it showed abnormal prominence of the left middle cardiac segment or if its size was 10 per cent greater than that predicted from the worker's height and weight.

Electrocardiograms were taken of all but a few patients, and minor degrees of axis deviation consistent with the patient's build were ignored. Because of the frequent occurrence of slurring of the QRS waves in normal persons,¹¹ this finding was also not regarded as abnormal.

It was not possible to perform red-cell counts of the blood in all cases. This was done only when there was a reason to suspect anemia clinically.

mur can be adequately evaluated without roentgenologic estimation of the heart size and an electrocardiogram

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SEROLOGIC TYPES OF HEMOLYTIC STREPTOCOCCI IN SCARLET FEVER IN MASSACHUSETTS*

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CONTINUING the study previously reported,¹ the hemolytic streptococci isolated from throat swabs of patients admitted to various Massachusetts hospitals with scarlet fever during 1944 were classi-

During the past year a total of 839 additional throat swabs were examined, of which 640 (76 per cent) were positive for Group A hemolytic streptococci. The methods employed in the type

TABLE 1 Distribution of Predominant Serologic Types of Hemolytic Streptococci in Cases of Scarlet Fever in Massachusetts, 1944

COMMUNITY	NO. OF CASES TYPED	FIRST		PREDOMINANT TYPES SECOND		THIRD		PERCENTAGE OF PREDOMINANT TYPES
		Type	Percentage	Type	Percentage	Type	Percentage	
Arlington	39	2	41	1	26	5	18	85
Boston	73	2	51	1	27	6	8	86
Malden	40	19*	35	2	35	1	2	70
Newton	22	2	64	17†	13	1	13	90
Somerville	41	2	41	1	39	6	7	87
Worcester	425	2	32	1	24	19*	14	70

*Weak cross-reaction with Types 4, 24, 26 and 29

†Cross-reaction with Type 23

fied as to serologic type. The laboratory studies were again done at the Department of Preventive Medicine and Epidemiology, Harvard Medical

classification of these strains were the same used for those referred to in the previous report. The distribution of the typed cases by age, sex and

TABLE 2 Distribution of Predominant Serologic Types of Hemolytic Streptococci in Cases of Scarlet Fever in Massachusetts, 1938-1944

COMMUNITY	YEAR	NO. OF CASES TYPED	FIRST		PREDOMINANT TYPES SECOND		THIRD		PERCENTAGE OF PREDOMINANT TYPES
			No	Percentage	No	Percentage	No	Percentage	
Boston	1938-1939 ²	340	15	45	13	4	11	3	52
	1939-1940 ³	35	2	55	6	11	—	—	66
	1942 ¹	19	2	69	19*	11	8	10	90
	1943 ¹	7	2	80	19*	20	—	—	100
	1944	73	2	51	1	27	6	8	86
Worcester	1942 ¹	34	2	63	19*	11	8	6	80
	1943 ¹	351	2	40	1	21	8	10	71
	1944	425	2	32	1	24	19*	14	70
Total of all communities studied	1942 ¹	69	2	57	19*	22	8	6	85
	1943 ¹	358	2	26	1	26	8	18	70
	1944†	640	2	36	1	26	19*	12	74

*Weak cross-reaction with Types 4, 24, 26 and 29

†Type 6 (7%) and Type 8 (6%) were fourth and fifth respectively in order of frequency

School, and arrangements for the provision of throat cultures were made through the co-operation of the Division of Communicable Diseases, Massachusetts Department of Public Health

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DISTRIBUTION OF TYPES

The percentage distribution of the predominant types of hemolytic streptococci isolated from scarlet fever patients in several Massachusetts communi-

||During the period 1942-1944 throat cultures in 1470 cases of scarlet fever were examined. Of these, 1067 (73 per cent) were positive for Group A streptococci.

frequent presence of left-axis deviation, which is related to the high incidence of hypertension

Significance of Laboratory Examinations

On hearing a systolic murmur, with no other abnormality present, it is a frequent practice for physicians to try to elicit a history of rheumatic fever, measure the blood pressure and attempt to explain

SUMMARY AND CONCLUSIONS

The clinical and laboratory findings of 91 full time employees with apical systolic murmurs are presented

In 71 (78 per cent) of these, the murmur was associated with significant cardiovascular abnormalities. Although this proportion increased slightly

TABLE 2 Significant Clinical and Laboratory Findings Related to the Age of the Patient

FINDING	AGE GROUP					
	BELOW 25 YR (28 CASES)		25-50 YR (35 CASES)		ABOVE 50 YR (28 CASES)	
	No	Per-centage	No	Per-centage	No	Per-centage
History of rheumatic infection	15	54	11	31	6	21
Hypertension	2	7	3	9	17	61
Roentgenologic enlargement	10	36	11	31	8	29
Abnormal electrocardiogram	7	25	12	34	19	68
PR interval greater than 0.2 sec	3		7		6	
Left-axis deviation	0		1		9	
ST and T abnormalities	4		3		5	
Low voltage of QRS	0		3		3	
QRS duration of 0.15 sec	0		0		1	
Miscellaneous*	0		2		2	
Total cases with at least one of above positive findings	21	75	23	65	27	96

the murmur clinically. If this is impossible, and especially if the murmur is faint, the patient is usually told that the murmur is of no significance. It was therefore considered important to report the x-ray and electrocardiographic findings in the patients who appeared negative by clinical examination (Table 3). This means that the patients had no rheumatic history, hypertension, tachycardia or fever and that there were no findings suggesting other disease that could produce a murmur. Although the incidence of abnormal laboratory find-

with the intensity of the murmur, faint murmurs were associated with these abnormalities in about 75 per cent of the cases showing them.

Almost all murmurs in the oldest age group (above fifty) were associated with other cardiovascular findings, most frequently with hypertension. In the younger age groups, the murmurs were less frequently significant, although positive findings were present in about 75 per cent of the cases. In the younger age groups, the murmurs were rarely associated with hypertension but often with a history

TABLE 3 Significant Roentgenologic and Electrocardiographic Findings in Patients with Clinically Negative Apical Systolic Murmurs

FINDING	DEGREE OF INTENSITY			TOTAL (39 CASES)
	FAINT (22 CASES)	MODERATE (9 CASES)	LOUD (8 CASES)	
Roentgenologic enlargement	4	1	4	9
Abnormal electrocardiogram	10	2	4	16
PR interval greater than 0.2 sec	6	1	2	9
Other abnormalities	6	1	3	10
Total case findings with at least one of above	12	3	5	20

ings was lower in such patients than in the group as a whole, half of them had enlarged hearts or abnormal electrocardiograms. These evidences of heart disease would have been completely missed without the more elaborate examinations. Furthermore, even when there were faint murmurs and no clinical findings, objective evidence of cardiac abnormalities was seen in half these cases. It is justifiable to conclude that no systolic murmur, regardless of intensity, can be adequately evaluated without thorough laboratory studies.

of rheumatic fever. The incidence of this history decreased as the age of the subjects increased.

Approximately half of 39 persons with apical systolic murmurs as the sole significant clinical finding had enlarged hearts roentgenologically or abnormal electrocardiograms. This was true even when the murmur was faint.

It is concluded that apical systolic murmurs are frequently associated with other cardiovascular findings, regardless of the intensity of the murmur, especially in patients over fifty. No systolic mur-

data on these families are combined with those on thirty-six families previously reported¹ It has been postulated that the diversity of types encountered in endemic scarlet fever may reflect the fact that the endemic disease, as it is known in this country, is the result of multiple introductions of various types of organisms, in contrast to outbreaks from a common source, which are usually due to a single serologic type⁸

Seasonal change has a profound effect on the incidence of scarlet fever, the seasonal variations

throughout the summer months It seems that the annual variations are determined by a secondary seasonal influence superimposed on the broader cyclic influence

The seasonal changes observed in streptococcus-carrier rates are similar to those of scarlet fever¹⁰ The seasonal fluctuations in the carrier rate are due to seasonal fluctuations in the prevalence of Group A strains, the other strains remaining at a more or less constant level throughout the year^{11, 12} The annual seasonal increase in the Group A carrier

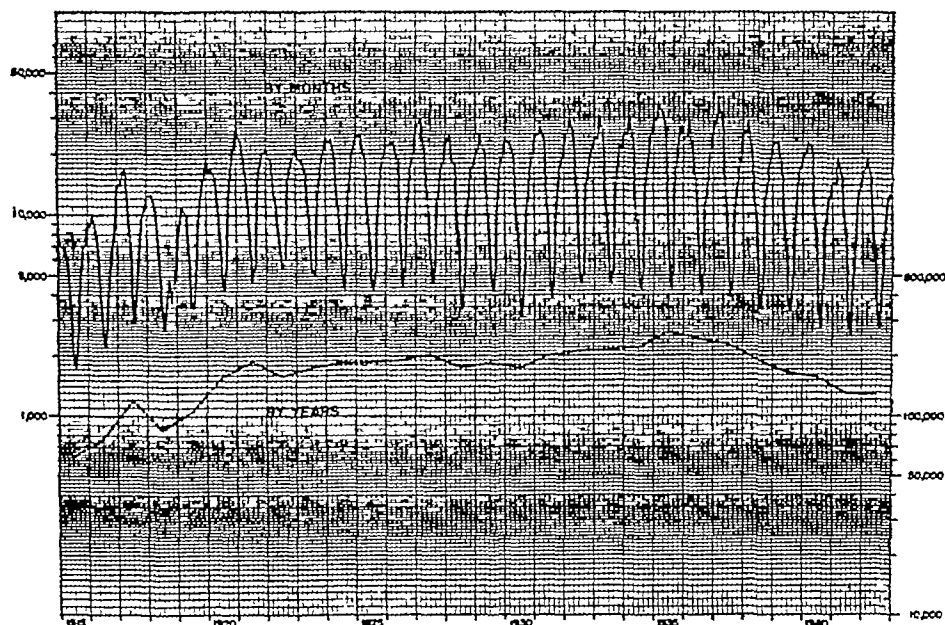


FIGURE 1 Incidence of Scarlet Fever in the United States Registration Area, 1915-1942
The data were obtained from Public Health Reports for the corresponding years

incidence for a given locality being remarkably regular In Massachusetts, for instance, during the period 1925-1939 distinct peaks of incidence occurred eleven times in March and twice in January and the low point of incidence was reached twice in July and eleven times in August

In addition to annual seasonal variations in incidence, scarlet fever presents some evidence of a broad cyclic movement over a period of years similar to that observed in other infectious diseases of bacterial origin⁹ In Figure 1 is plotted the monthly incidence of scarlet fever in the United States Registration Area for the years 1915-1942 The regularity with which the points of high and low incidence undulate indicates not only that the high and low points in a single year are related, but also that the total incidence in a given year is related to that in the preceding year and in turn influences the incidence in the following year It should be noted that the incidence of scarlet fever does not approach zero during the season of lowest incidence but continues to occur in sizable numbers of cases

rate has been interpreted as a precursor of streptococcal infection, but it has not yet been established that an increased carrier rate is the cause rather than the result of streptococcal disease Certainly the coincident seasonal changes in the incidence of scarlet fever and the Group A carrier rate suggest the influence of a basic phenomenon common to both

The distribution of the predominant types of hemolytic streptococci isolated from scarlet fever occurring in a single Massachusetts community during the epidemic year 1943-1944 is plotted in Figure 2 The incidence of either Type 2 or Type 1 varied with the progression of the seasons in the same manner as does the incidence of scarlet fever in the United States Registration Area As can be seen from the curves in this figure, the rates of increase and decrease during the period of observation were the same for both these types Additional analyses indicate that the same was true of the other less prevalent serologic types during the same period As was recently pointed out,¹³ the similarity

ties is presented in Table 1. The consistency of the frequency with which certain types were recovered from the majority of cases in different localities is noteworthy. In Table 2, the data concerning types of streptococci prevalent in two Massachusetts communities for successive years are compared with those for the entire sample typed in the present studies during the period 1942-1944. The additional data presented in Table 2 lend support to the observation previously recorded *viz*, in the period studied certain types tended to maintain themselves as the cause of scarlet fever in a large proportion of cases.¹

SCARLATINAL AND NONSCARLATINAL INFECTIONS

Since these studies were done on patients admitted to infectious-disease hospitals, there was but limited opportunity to study nonscarlatinal infections. An occasional swab, however, was received from a patient admitted to the hospital for one reason or another with a streptococcal infection other than scarlet fever. A total of 44 cultures from such cases were studied. Of these, 33 (75 per cent) were positive for Group A hemolytic streptococci. The frequency with which the various serologic types were encountered may be compared with the frequency with which these and other types were isolated from patients with a clinical diagnosis of scarlet fever (Table 3). Two important and often

TABLE 3 Frequency of Serologic Types of Hemolytic Streptococci in Cases of Scarlet Fever and of Other Streptococcal Infections in Massachusetts, 1942-1944.

SEROLOGIC TYPE	PERCENTAGE INCIDENCE	
	SCARLET FEVER	OTHER STREPTOCOCCAL INFECTIONS
2	36 6	30 3
1	23 9	21 2
19*	12 1	18 2
8	11 0	3 0
6	6 3	
17†	3 6	12 1
25	1 5	6 0
5	1 2	
12	0 9	3 0
29*	0 7	3 0
27	0 4	3 0
4*	0 3	
11	0 3	
14	0 3	
18	0 3	
13	0 2	
15	0 2	
10	0 1	
24*	0 1	

*Serologically related with the serums used

†Cross-reaction with Type 23

neglected points are illustrated in this small series. In the first place, there is no single serologic type peculiar to the clinical diagnosis of scarlet fever. Secondly, a predominant type can be recovered from patients with nonscarlatinal infections with the same degree of frequency with which it is found in scarlet fever. It thus appears that in this series of cases the factor that determines one clinical syndrome or another is not the type of streptococcus but probably differences in susceptibility or resistance to erythrogenic toxin (common to most types of streptococci), as has previously been pointed

out by Gordon.⁴ Age is a factor that determines in part the host reaction to erythrogenic toxin. Of the patients in this study with a diagnosis of scarlet fever, 83 per cent were less than fifteen years of age, compared with 15 per cent of those with a diagnosis other than scarlet fever.

SEROLOGIC TYPE

These studies are perhaps still too limited to support any sweeping conclusions concerning the geographic limitations and constancy of a serologic type pattern in scarlet fever. It is of interest, however, that in five of the six communities from which samples were obtained during 1944, Types 2 and 1 were predominant causes of scarlet fever. The available evidence suggests that the Type 2 organism has maintained itself predominantly in scarlet fever in Massachusetts since 1939-1940 (Table 2). Type 1 appeared in appreciable numbers of cases in 1943, replacing Type 19. Despite the fluctuation in relative frequency, the percentage of scarlet fever that could be attributed to two or three predominant types remained fairly constant from year to year during the period of study.

The movement of a particular serologic type of hemolytic streptococcus is difficult to follow in a community of any size. Since dissemination can be accomplished by the carrier as well as by the patient, it is usually impossible to determine the exact epidemiologic relation between cases of endemic scarlet fever. In the present study, spot maps prepared according to serologic type by street address in a large community failed to reveal any significant grouping of cases by type. On the other hand, the results of family studies⁵ and schoolroom studies^{6, 7} indicate that if the population group can be broken down into basic epidemiologic units amenable to complete study, the movement of a given serologic type can be followed. For example,

TABLE 4 Serologic Types of Hemolytic Streptococci Isolated from Multiple Cases of Scarlet Fever and Other Streptococcal Infections in 97 Families in Massachusetts, 1942-1944.

SEROLOGIC TYPE	NO. OF PRIMARY AND CO-PRIMARY CASES	NO. OF SECONDARY CASES
2	38*	27†
1	27*	20
8	10	12
6	16	10
19†	8‡	5
5	1	1
15	1	1
12	2	0
17¶	1	1
14	1	1
Totals	106	78

*One case of septic sore throat.

†One case of abscessed finger.

‡Weak cross-reaction with Types 4, 24, 26 and 29.

§Two cases of streptococcal meningitis.

¶Cross-reaction with Type 23.

during the past year the serologic types of hemolytic streptococci isolated from multiple cases of scarlet fever and other streptococcal infections occurring in sixty-one families were obtained. The strains isolated from multiple cases in each household were of the same serologic type. In Table 4 the

SUMMARY

Types of hemolytic streptococci associated with scarlet fever in certain Massachusetts communities during 1944 were predominantly, in order of frequency, Types 2, 1, 8 and 19. Similar type distributions were obtained in the study previously reported for 1942-1943. During the three-year period of this study, there was some shifting of type in relative order of frequency, but Type 2 seemed to maintain itself as a major cause of scarlet fever.

During the course of this study, 1067 cases of scarlet fever were classified with respect to the serologic type of the streptococcus, 19 types being encountered. The frequency with which a given type was isolated from cases of nonscarlatinal infection was essentially the same as that in cases of scarlet fever. Additional observations on multiple cases in the same family indicate that household outbreaks are usually due to a single serologic type.

Spatial relations could not be demonstrated among cases of scarlet fever due to the same serologic type except in basic units of population, such as a family. A study of the seasonal distribution of the predominant types in scarlet fever indicated that the prevalence of a particular type fluctuated with season in a manner similar to that of scarlet fever. A study of the incidence of scarlet fever in the United States Registration Area over a period of years suggests that annual seasonal variations are superimposed on a broad cyclic movement covering a period of years.

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of two distributional curves suggests the operation of the same factor producing the identical result in each. The obvious factor common to both Types 2 and 1, as well as to other serologic types, is seasonal change rather than some ill-defined difference in the ability of certain types to acquire new hosts.

DISCUSSION

The original purpose of Griffith's¹⁴ serologic investigations was to establish that scarlet fever

if indeed it is a parasitic rather than a host factor is not entirely dependent on differences in type or even in group antigens, but more probably on some common denominator that exists irrespective of serologic characteristics. Evidence is accumulating that the ability to produce human disease is not peculiar to Group A strains alone. Infections due to other groups of streptococci are admittedly rare as compared with Group A infections, but they do occur.¹⁵⁻²¹ Such infections are usually nonrespiratory

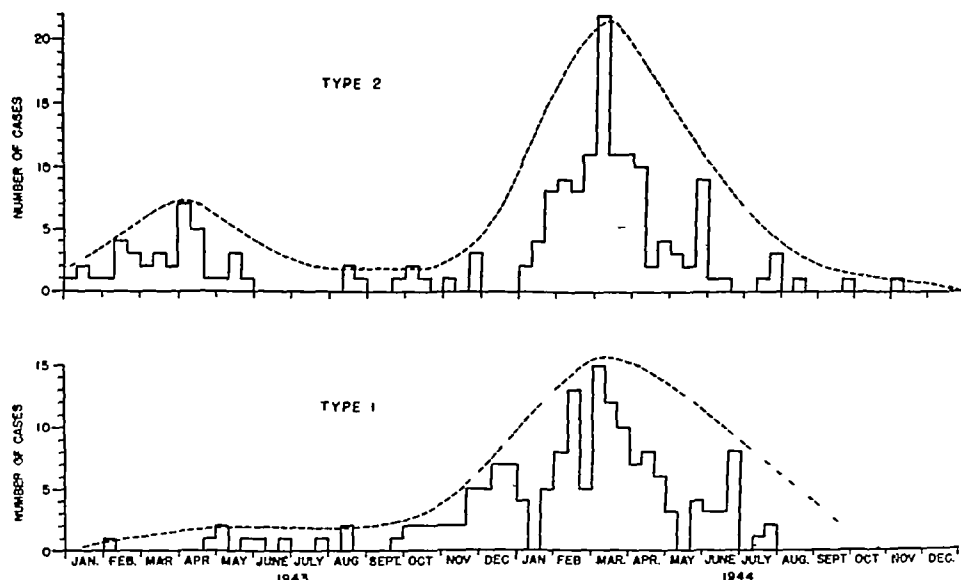


FIGURE 2 Annual and Seasonal Variations in Certain Serologic Types of Hemolytic Streptococci in Scarlet Fever Occurring in a Single Community, 1943-1944.

The figures do not include multiple cases in the same household

is or is not produced by a distinct species of hemolytic streptococcus. The accumulated evidence of the occurrence of all Griffith's types in scarlet fever, as well as in other streptococcal infections, has established the essential unity of streptococcal disease in general. The observation that the com-

tory in origin, such as the cases recorded in Table 5. Recent studies on the relation of hyaluronic acid to the virulence of Group C²² and Group A hemolytic streptococci²³ support the hypothesis that serologic characteristics may be incidental to pathogenicity. Indeed, the everyday observation that all serologic types can produce the same clinical syndrome in itself supports the existence of a common denominator for all types.

Although studies on the antigenic difference among the streptococci have not yet contributed substantially to knowledge of the fundamental mechanics of streptococcal infection, they have provided the epidemiologist with a means of studying related cases of this group of diseases. Either the M-precipitin²⁴ or the slide-agglutination¹⁴ technique, when properly applied to the study of an outbreak, can add valuable information to the study. From an epidemiologic viewpoint, it seems to matter little which method is used, since either provides only a means of identifying the movement of a particular strain.[†]

†In view of the current observations on discrepancies in the results obtained with the two methods it may be pointed out that since the two techniques can involve different antigen-antibody systems, any degree of correlation should not be expected with sera prepared and standardized against different type antigens.

TABLE 5 Streptococci Other than Group A Isolated from Cases of Human Infection *

CLINICAL DIAGNOSIS	SOURCE OF CULTURE	GROUP
Meningitis	Spinal fluid	B
Meningitis	Spinal fluid	B
Urinary infection	Catheterized urine	B
Sepsis	Blood	D
Sepsis	Blood	D
Sepsis	Blood	E
Empyema	Fluid from surgical drainage	F
Empyema	Fluid from surgical drainage	F
Empyema	Fluid from surgical drainage	G

*In each case streptococci were present either in pure culture or in pre-dominant numbers.

mon erythrogenic toxin is broadly valent to nearly all serologic types explains the heterogeneity of types encountered in scarlet fever. These and similar observations suggest that the disease-producing capacity of the hemolytic streptococcus —

highly acid glomerular filtrate. The capacity of the tubules to selectively reabsorb water and chlorides is lost, and urea and potassium are retained. The retention of potassium, coupled with its continued escape into the blood stream from the damaged muscle, leads to toxic plasma levels, eventual cardiac arrest and death.

Bywaters and Popjak¹⁰⁰ and Bywaters and Stead¹⁰¹ attempted to establish the comparative importance of compression, of muscle necrosis and of myoglobinuria in the production of renal failure. Their experimental work was performed on rabbits that had almost no myoglobin in their muscles, and it was necessary to infuse solutions of human myoglobin to produce myoglobinuria. It was found that crushing injury to muscle produced shock and transitory azotemia but not renal failure. Myoglobinuria caused no ill effects in normal rabbits but resulted in severe renal damage, uremia and death in animals in which severe acidosis or crushing injury had been produced. Autopsy of these animals showed kidney lesions similar to those noted in fatal human cases of the crush syndrome.

In contrast to these findings are the previously described observations of Bing,³¹ who found that injections of solutions of pure dog myoglobin produced no significant abnormality in the renal function of normal or acidotic dogs. This does not exclude the definite probability that myoglobinuria occurring in patients in a state of shock, as well as in acidosis, may severely damage the kidneys. Furthermore, it must be emphasized that observations made in one animal species are not necessarily applicable to another species or to man.

Although the crush syndrome and myoglobinuria were first described in the English literature in 1941, the condition was recognized by the Germans during World War I and their observations were summarized by Minami.¹⁰² It is probable that the syndrome follows many different types of trauma — for example, automobile and industrial accidents — and that it is not recognized because attention is focused on the surgical aspects of the injuries.⁹⁷

Prophylactic measures to prevent renal damage are of the utmost importance in caring for persons who have been victims of compressing and crushing injuries. Prior to the release of the pressure, or as soon thereafter as possible, it appears advisable to administer transfusions of blood or plasma and to give fluids in amounts adequate to maintain a relatively normal circulating blood volume and good urinary flow. Judicious use of alkalies is probably advisable in an attempt to maintain an alkaline urine reaction.

Treatment of a patient with the crush syndrome once it is fully developed appears to have little influence on the eventual outcome of the case. The administration of large amounts of alkali in the face of already established oliguria is of little value and may actually be harmful.³⁴ Every attempt

should be made to maintain the concentration of blood electrolytes as normal as possible — a difficult task in view of the tendency to accumulate potassium. Bywaters⁹⁷ states that the administration of insulin and dextrose to these patients may reduce the blood potassium level and may improve the cardiac function.

PARALYTIC MYOGLOBINURIA AND HAFF DISEASE

Paralytic myoglobinuria is an extremely rare disease of man, only 8 cases having been reported.¹⁰³ It occurs not infrequently in work horses, however, and is said to be well known to veterinarians.¹⁰⁴ The symptoms are similar in men and horses. The disease affects previously healthy individuals who have been inactive for a few days but who have continued to eat the same diet that they consumed when performing heavy physical exertion. On returning to work they develop stiffness and lameness of one or more muscle groups, rapidly lose strength and are soon paralyzed. Twitching of the muscles is often noted. Chills and fever occur, and dark red urine is passed. Renal failure and uremia similar to that described in the crush syndrome sometimes develop and may prove fatal in five or six days. The plasma potassium concentration becomes markedly elevated.¹⁰⁵ If death does not occur, there may be residual paralysis of the affected muscle groups. Repeated attacks are frequent in nonfatal cases.¹⁰⁶

The pigment passed in the urine has been identified as myoglobin.^{106, 107} Autopsied cases show edematous, pale muscles, which are described as looking like "fish flesh." The kidneys show tubular degeneration and myoglobin casts and are similar in appearance to those found in patients dying of the crush syndrome.¹⁰⁸

It has been postulated by Carlström¹⁰⁷ that the cause of the disease is damage to the muscle cells by the sudden release of large amounts of lactic acid. Excessive amounts of glycogen are stored in the muscles during rest, and on return to activity this glycogen is converted to lactic acid so rapidly that it cannot be removed by diffusion. It consequently accumulates in the muscle cells in such a high concentration that the cells are damaged, myoglobin, potassium and creatine readily diffusing into the blood stream. Minetti¹⁰⁴ produced the disease experimentally by feeding resting horses a high-carbohydrate diet and then exercising them, tending to confirm Carlström's hypothesis.

A somewhat similar condition, known as "Haff disease" and characterized by paroxysmal attacks of severe pain, stiffness and limitation of motion of the striated muscles and the passage of red or black urine, has been described in inhabitants living near the sea inlet or *Haff* in Königsberg, Germany.¹⁰⁸ The urinary pigment has been identified as myoglobin,¹⁰⁹ and autopsied cases showed necrotic striated muscles that looked like "fish flesh." The disease is supposedly caused by ingestion of fish

MEDICAL PROGRESS

HEMOGLOBINEMIA AND THE HEMOGLOBINURIAS (Concluded)*

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BOSTON

MYOGLOBINURIA AND THE CRUSH SYNDROME

During the blitz on London in 1940, English physicians began to see air-raid casualties who developed an unusual and highly fatal form of renal failure.⁹⁷ All these patients had been buried under rubble for a period of hours, and usually one or more extremities had been crushed or severely compressed by heavy timbers or masonry. Many of these persons appeared to be in good general condition soon after release from compression, but after an hour or two the signs of vascular collapse or shock developed, with pallor, cold perspiration, a weak, thready pulse and a precipitous drop in blood pressure. The traumatized limb became greatly swollen, paralyzed and insensitive, and on operation large masses of muscle were found to be necrotic. Restoration of blood volume by transfusion of plasma or blood usually restored the blood pressure to normal, the signs of shock disappeared, and the patients appeared to be well on the way to recovery. This improvement and the good subjective appearance of these patients were most deceptive, however. The volume of urine excreted became smaller and smaller, signs of extreme renal failure appeared, the blood urea concentration rose to high levels, the blood pressure became elevated, and death usually occurred quite suddenly on the sixth or seventh day after the initial injury.

Urine voided after release of the compression was "smoky," brown or occasionally red and often contained a heavy brown precipitate. Spectroscopic examination of these urines showed no hemoglobin or methemoglobin but oxymyoglobin and metmyoglobin.⁷ The brown precipitate was identified as acid hematin. All the urines were highly acid with the reaction as low as pH 4.6.⁹⁷ Excretion of myoglobin usually continued for one or two days, but casts containing granules of acid hematin could be demonstrated in the urine for five or six days more.

The volume of urine excreted progressively decreased, its composition becoming similar to that of glomerular filtrate: the urea concentration was low, although the blood urea was high, the chloride content was high although the plasma chloride was low and, finally, reducing substances appeared.⁹⁸

Bywaters and Dible⁹⁹ attributed these changes to almost complete loss of tubular function and suggested that the small volume of urine could be accounted for by leakage of glomerular filtrate into the blood stream through the damaged tubules. Potassium and creatinine presumably derived from the damaged muscle were present in high concentration in the first specimens of urine voided after release of the compression.

In two thirds of the 100 cases reported the patient died, usually on the sixth day. The circumstances of death were suggestive of fatal potassium poisoning, with death from cardiac irregularity. Electrocardiographic abnormalities were similar to those noted in potassium poisoning, and the concentration of potassium in the serum was more than twice the normal value.⁹⁷ The accumulation of large amounts of potassium in the plasma brought about by two mechanisms: the release of large amounts of potassium from the damaged muscle and the failure of the kidneys to excrete adequate amounts because of oliguria and failure.

At autopsy the kidneys showed the picture frequently found in cases of intravascular hemolysis. The glomeruli were normal, but the epithelial cells of the convoluted tubules were necrotic, many tubular lumens contained brown casts of myoglobin.⁹⁹ Studies of the traumatized muscle showed that large masses of muscle were pale, flabby, looked like "fish flesh" and were necrotic. Most of the myoglobin, potassium, phosphorus, creatine and glycogen had been lost from the muscle.⁹⁷

The sequence of events and the pathogenesis of the crush syndrome may be summarized as follows. Because of the crushing injury, or prolonged anoxemia, a mass of muscle is so badly damaged that it becomes necrotic. On release of the compressing force, plasma escapes into the traumatized area, frequently in large enough amounts to produce a critical decrease in the circulating blood volume, with consequent shock. The intracellular constituents of the damaged muscle cells, notably myoglobin, potassium, creatine and acid metabolites, escape into the blood stream, and the decreased blood volume and hypotension are added to the complicating factors of acidosis, a toxic plasma concentration of potassium, myoglobinemia and myoglobinuria. The combination of these factors results in decreased glomerular filtration, tubular necrosis and precipitation of myoglobin casts in

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globin in the plasmas of 9 of 21 cross-country runners and of 18 of 22 marathon runners on completion of their races. Three of the marathon runners showed frank hemoglobinuria. Other observers have also reported a high incidence of hemoglobinemia and hemoglobinuria after long-distance runs and forced marches.^{117, 118} Persons with march hemoglobinuria probably develop this physiologic hemolysis during less strenuous exercise than usual and, because of a lowered renal threshold for hemoglobin, readily show hemoglobinuria. Their lowered renal threshold may be a reflection of a moderate tubular blockage by hemoglobin breakdown products that has been brought about by the frequent occurrence of subthreshold levels of hemoglobinemia necessitating the frequent tubular reabsorption of hemoglobin. The mechanism by which erythrocytes are destroyed in normal persons during severe exertion or in patients with march hemoglobinuria during moderate exertion remains unexplained.

FAVISM

Favism is a form of acute hemolytic anemia and hemoglobinuria caused by the ingestion of the green seeds of the fava bean (*Vicia faba*) or by the inhalation of its pollen. It occurs most frequently on the island of Sardinia, where it is stated by Luisada¹¹⁹ that many thousands of cases occur every year. The disease is also fairly common in Sicily and in some districts of the Italian mainland. It is exceedingly rare in the United States, only 3 cases having been reported.¹²⁰⁻¹²² This is in spite of the fact that considerable quantities of fava beans are consumed in the United States. The high incidence of the disease in Sardinia, Sicily and Calabria has been explained on the basis of increased racial susceptibility, since the inhabitants of these areas are said to have kept more of the "typical characteristics of the 'original' Mediterranean race" than have the other Italian peoples, who are less susceptible to the disease.¹¹⁹ In 20 per cent of the cases a hereditary factor apparently plays an important role in predisposing to the disease. Certain families have been described in which every member for several generations developed the condition.¹²⁰ Attacks may occur in either sex and at any age, but are most serious in infants and children, in whom the mortality may reach 8 per cent. A person may experience repeated attacks.

The attacks may occur a few minutes to several hours after inhalation of the pollen or ingestion of the bean. The symptoms are those of rapid intravascular hemolysis, with chills, fever, vomiting, pain in the back and rapidly progressing anemia. Blood destruction may be so extreme and occur so rapidly that death from anemia occurs within twenty-four to forty-eight hours. Hemoglobinuria appears within a few hours of onset and may persist for several days. Jaundice develops after a few

hours and may be intense. After the acute hemolytic episode there is rapid blood regeneration.

Oliguria, renal failure, uremia and death occasionally follow the hemoglobinuria. Studies of the blood have failed to reveal any changes in erythrocyte fragility, and the serum contains no abnormal hemagglutinins or hemolysins.¹²⁰⁻¹²²

Investigations of the etiology and pathogenesis of favism have not been extensive, and many of the reported studies have been poorly conceived and inadequately controlled. The disease is supposedly caused by an allergic response to the protein of the fava bean. A person may eat these beans for many years and suddenly develop an attack from the ingestion of a single bean. Milk from a goat fed on fava beans is reported to have contained enough of the antigenic material to produce a typical attack.¹¹⁹ Fresh raw beans are more likely to cause the disease than dried or cooked ones. Approximately one third of the cases result from inhalation of the pollen from the blooming plants.

Allergy to the products of the fava bean manifests itself in skin sensitivity, as well as in the acute hemolytic reaction. Desensitization of the skin is reported to occur during the hemolytic reaction and may not reappear for several weeks.^{119, 122}

Attempts to prove the allergic nature of the disease experimentally in rabbits were complicated by the direct hemolytic effect of the bean and its extracts on the animals.¹¹⁹ The possible existence of a hemolytic agent in the bean is of considerable interest. As suggested by Ham and Castle,¹²³ a hemolytic agent in the fava bean may act in a fashion similar to the strongly hemolytic substance concanavalin A, which is derived from the fruit of another fabaceous plant, the jack bean. If such a hemolytic substance could be shown to exist in the fava bean, it would explain the pathogenesis of favism.

HEMOLYTIC TRANSFUSION REACTIONS

Hemolytic reactions to blood transfusions are unfortunately much more frequent and of far greater seriousness than is usually suspected. In a collected series of 43,284 transfusions, the incidence of hemolytic reactions was 1.8 per 1000 transfusions and the mortality was 1.4 per 1000 transfusions.¹²⁴ This mortality rate places the risk of blood transfusion in the same range as the risk of some major operations, a fact that is seldom recognized.

Hemolytic transfusion reactions are almost always the result of transfusion of intergroup¹⁶⁻¹⁸ or Rh incompatible^{125, 126} blood. Occasionally they may be due to the use of blood that is contaminated with bacteria or to blood that has been stored too long or in an improper fashion — for example, at the wrong temperature.

Following transfusion of incompatible blood there occur rapid intravascular agglutination and hemolysis of the donor cells, with resultant hemo-

or eels poisoned with resinous acid wastes discharged into the inlet from the nearby cellulose factories. Stoeltzner¹⁰⁸ has experimentally produced the disease in cats by poisoning fish with these resinous acids and by feeding the fish to the cats, which promptly developed acute muscle necrosis and myoglobinuria.

MARCH HEMOGLOBINURIA

March hemoglobinuria is the only condition in which the appearance of hemoglobin in the urine does not indicate serious systemic disease. It occurs exclusively in healthy, young adult men and is precipitated by walking or running but not by other types of physical exertion. Nor is it related to chilling, fever, sleep, hyperventilation or local hemostasis, as Gilligan and Blumgart¹¹⁰ have demonstrated. There is no associated disease or physical abnormality, and no racial or familial predisposition. It usually is entirely asymptomatic except for the appearance of red urine following a period of walking or running, occasionally the subject may experience aching or drawing pain in the lower back or abdomen.^{111, 112} Hemoglobinuria persists for a few hours following exertion in most cases, but it may last for several days in rare cases.¹¹³ The spleen has been noted to increase in size following attacks in 1 case,¹¹⁰ and similar enlargement of the liver has been described in 2 cases.^{110, 114}

The type of exertion and the posture of the subject are most important in producing attacks of march hemoglobinuria. With the exception of a case described by Witts⁶⁶ in which bicycling as well as walking produced attacks, hemoglobinuria occurs only after walking or running. Other types of exertion, such as wood chopping, bicycling or arm exercise, produced no hemoglobinuria, although the exertion was greater than that which would have been required to produce hemoglobinuria by walking, furthermore, prolonged standing or reclining in a lordotic position never caused hemoglobinuria.¹¹⁰ Although the majority of patients have had no postural abnormality, some have demonstrated an exaggerated lumbar lordosis that has been suspected of being responsible for the attacks.^{66, 112, 114, 115} In 2 cases, the obliteration of the normal lumbar curve and the production of a slight kyphosis by the application of a plaster cast served to prevent the development of hemoglobinuria after an amount of exercise that otherwise would have produced an attack.^{110, 114} In one of these cases in which the plasma hemoglobin was investigated, not only did the kyphotic position prevent the appearance of hemoglobin in the urine but it also prevented any increase in plasma hemoglobin, indicating that the change in posture in some way prevented the occurrence of hemolysis. This highly significant observation suggests that some vascular or circulatory abnormality may be responsible for the hemolysis, but as Gilligan and Blumgart¹¹⁰ point out, there is no

definite evidence that there is any such abnormality.

March hemoglobinuria is self-limited, and ery usually occurs without treatment within months or one or two years, although it occasionally last longer. Witts⁶⁶ reported a case of occasional attacks during a seven-year period. Foerster¹¹⁶ described a patient with attacks twenty years.

Relatively little was known of the pathophysiology of march hemoglobinuria until the excellent studies of Gilligan and Blumgart,¹¹⁰ who investigated 3 cases and summarized the observations on all reported cases. Although the attacks are precipitated by muscular activity, the hemoglobin excreted in the urine is not myoglobin from the muscles but oxyhemoglobin derived from the blood. Hemoglobinemia always precedes the appearance of hemoglobin in the urine, and after exertion may occur without hemoglobinuria. The renal threshold for hemoglobin is considerably higher than that in normal persons. The amount of hemoglobin excreted during attacks usually does not exceed 40 cc and is invariably too small to produce anemia.

There is no abnormality in the blood to account for the increased hemolysis. The erythrocytes and platelets are normal in number and morphology. The fragility of the erythrocytes is normal, and no abnormal agglutinins or hemolysins are present in the serum.

Kidney function is normal and is not influenced by attacks, although small quantities of hemoglobin may appear in the urine when there is hemoglobinuria.

Gilligan and Blumgart¹¹⁰ have done much to clarify the etiology of march hemoglobinuria by reviewing the various theories concerning its cause; they have shown that the belief that it is related to paralytic myoglobinuria^{111, 116} is unfounded. The pigment excreted is hemoglobin and not myoglobin. There is no evidence to support the suggestion that hemolysis occurs in the kidneys, but rather as a result of hemolysis in the renal vein, and that the majority of the released hemoglobin is excreted in the kidneys.⁶⁶ Indeed, only 10 per cent of the liberated hemoglobin appears in the urine. The importance of the standing posture and the occurrence of lumbar lordosis in a few cases has been pointed out by Fisher and Bernstein¹¹² to associate the mechanism of production of march hemoglobinuria with the orthostatic albuminuria. Patients with orthostatic albuminuria do not have hemoglobinuria, however, and prolonged standing without exercise does not cause albuminuria in subjects who develop march hemoglobinuria on exertion.¹¹⁰

Gilligan and Blumgart¹¹⁰ offer what seems to be the most logical explanation of the disease. They suggest that it is merely an accentuation of a physiological hemoglobinemia and hemoglobinuria that occurs in normal, healthy persons following extremely vigorous and prolonged exertion. They have demonstrated increased concentrations of hemoglobin in the blood during attacks.

changes have been detected in cases that were studied early in the course of the acute hemolytic process¹³⁴⁻¹³⁷ In other cases abnormal hemagglutinins have been demonstrated,^{134, 135, 138, 139} but these may have been produced by the underlying disease process rather than by the sulfonamide itself. How sulfonamides produce osmotic fragility changes or abnormal hemagglutinins and what part these abnormalities play in the production of the hemolytic process are unknown.

Hemoglobinuria practically very rarely occurs in familial hemolytic jaundice, even during acute crises with massive blood destruction. It is probable that the reticuloendothelial system is continually hyperactive in these cases and is therefore able to metabolize erythrocytic breakdown products readily in times of acute hemolysis. Hemoglobin occasionally appears in the urine in acute hemolytic anemia of the acquired type, and isohemolysins have been demonstrated in the serums of some of these patients.¹⁴⁰

Quinine taken in extremely large doses as an abortifacient has produced fatal hemolytic anemia, with hemoglobinuria, in 10 cases.^{141, 142} How quinine causes hemolytic anemia is poorly understood. Studies by Ponder and Abels¹⁴³ have shown that it exerts a hemolytic effect in vitro only in concentrations that are far in excess of therapeutic blood levels. It is unlikely that even the large doses taken by patients who have died produced blood levels sufficiently high to cause hemolysis. An abnormal susceptibility of the erythrocytes of pregnant women to hemolysis by quinine has been postulated,¹⁴⁴ but this has never been demonstrated and seems improbable.

The bites of certain snakes^{144, 145} and spiders¹⁴⁶ produce increased osmotic fragility, rapid intravascular hemolysis and massive hemoglobinuria as a result of the direct chemical action of the venom on the lipids of the red cell. A similar lytic effect of the toxin of *Clostridium welchii* probably accounts for the hemolytic anemia and hemoglobinuria of such infections.

Arsine (arsenuretted hydrogen) is a highly toxic gas that produces extreme intravascular hemolysis, profound anemia, methemoglobinemia, hemoglobinemia and hemoglobinuria. It is not used industrially but may be generated inadvertently in any process in which an acid or a metal, either or both of which contain arsenic, are brought into contact, with the resultant evolution of nascent hydrogen and the interaction of the hydrogen and arsenic to form the gas. Acute poisoning has occurred most frequently in chemical laboratories, galvanizing plants, submarines (from arsenic in lead storage-battery plates), ships carrying ferrosilicon and factories that manufacture hydrogen gas from zinc.¹⁴⁷ Three cases occurring in laborers unloading fish-scrap fertilizer from the holds of ships have recently been reported.¹⁴⁸ Arsine has two effects on

the blood. It rapidly produces methemoglobin and more slowly is metabolized to some as yet unidentified compound that produces extreme intravascular hemolysis. A latent period varying from a few hours to two days may follow inhalation of the gas before the hemolytic process begins. Once started, however, hemolysis may progress so rapidly that death from anemia occurs within a few hours. In patients surviving the acute hemolytic phase, posthemoglobinuric anuria sometimes develops and death may result from renal failure and uremia.^{148, 149}

Hemoglobin must remain in its normal intravascular position if health and normal body function are to be maintained. Although capable of transporting oxygen and of sustaining life when in solution in the plasma,^{150, 151} the escape of large quantities of hemoglobin from erythrocytes into the plasma is almost invariably followed by adverse symptoms and hemoglobinuria and frequently by death. Red or black urine, the danger signal indicating extensive intravascular hemolysis, must always be taken seriously, its cause determined and appropriate therapeutic measures immediately instituted.

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globinemia, hemoglobinuria, chills, fever, profuse perspiration, nausea, vomiting and severe pains in the lower back. Occasionally there may be no subjective symptoms whatever, and rarely transfusion of incompatible blood may not cause serious complications.¹²⁷ The usual course of events in at least half the cases of incompatible transfusions is oliguria, anuria, uremia and death.^{16, 124, 128}

The danger of using a Group O, the so-called "universal," donor, has recently been re-emphasized by Malkiel and Boyd,¹²⁹ who reported that transfusions of Group O, Rh compatible blood into a Group A recipient resulted in a severe reaction, with the destruction of 30 per cent of the recipient's cells. The donor blood was found to have a high concentration of anti-A agglutinin, which accounted for the destruction of the recipient's cells. In other reported cases, transfusion of compatible Group O blood has produced fatal hemolytic reactions.¹²⁸

As previously discussed, the actual pathogenesis of the tubular degeneration and renal failure in these cases is not definitely established. In all probability they result from a lowered blood pressure, vasoconstriction of renal blood vessels, markedly reduced renal blood flow, lowered alkali reserve and the secretion of large amounts of hemoglobin or hemoglobin derivatives in a highly acid urine.

The treatment of hemolytic transfusion reactions is unsatisfactory, and it is far better to avoid the necessity for such treatment by establishing, unequivocally, the group and Rh compatibility of the donor and the recipient before transfusion. Care must also be exercised that bank blood has been stored under the proper conditions, and that the period of storage has not been too long.

The extreme seriousness of hemolytic transfusion reactions and the fact that about half the patients developing anuria die make it absolutely essential that effective therapeutic measures be instituted immediately in any patient suspected of having such a reaction. Retransfusion of fresh compatible blood as soon as possible after the reaction has occurred is probably of benefit, since it increases renal blood flow and promotes glomerular filtration.³³ Hesse¹³⁰ states that in 16 patients treated in this way, there were only 2 deaths, and in one of the latter, retransfusion was not performed until the sixth day. It also is advisable to maintain the blood electrolytes and alkali reserve as normal as possible and to try to keep the urine alkaline,¹³¹ although excessive amounts of alkali should not be administered.³⁴ Procedures such as decapsulation of the kidneys, lavage of the renal pelves and sympathectomy probably are not therapeutically effective.

THE HEMOGLOBINURIA OF BURNS

Severely burned patients frequently develop hemoglobinuria and may show evidences of renal failure with renal lesions similar to those observed in other forms of intravascular hemolysis. The ap-

pearance of hemoglobinuria in a burned patient is a grave prognostic sign, not so much because of the severity of the hemolytic process, which rarely produces marked anemia, but because it is an indication that the burn is both extensive and serious in degree. Of the 10 burned patients with hemoglobinuria studied by Shen, Ham and Fleming¹³² only 1 survived. One of Cope and Rhinelander's¹³³ 9 patients died.

The pathogenesis of the hemoglobinuria of burns has been explained by the excellent investigations of Shen, Ham and Fleming.¹³² They observed that for several hours after the burn the blood of severely burned patients contained numerous spherocytic and fragmented erythrocytes and that the presence of these abnormal cells was reflected by a marked increase in the osmotic fragility of the erythrocytes. The number of abnormal red blood cells and the fragility changes progressively decreased after the burn as the abnormal cells were destroyed. By heating normal blood *in vitro* to a temperature of 51 to 65°F, they produced marked morphologic and fragility changes that were directly attributable to the effect of heat on the cells themselves and were not due to abnormalities produced in the plasma. When previously heated blood was transfused into normal dogs, hemoglobinemia and hemoglobinuria occurred and the changes in the appearance of the erythrocytes and in the osmotic fragility were identical with those seen in severely burned human patients.

The cause of burn hemoglobinuria is thus readily explained. At the time the burn is inflicted, the temperature of the burned tissue reaches or exceeds 51°C and the blood passing through these tissues is heated to a similar temperature. The heat produces irreversible changes in the erythrocytes, and these cells are subsequently rapidly destroyed, with the production of hemoglobinemia and hemoglobinuria.

TOXIC HEMOGLOBINURIAS

Any toxin or process that destroys erythrocytes rapidly enough produces hemoglobinemia and hemoglobinuria. Thus, hemoglobinuria is occasionally seen in almost any type of acute hemolytic anemia. The number of toxic agents that are hemolytic is large, and only a few of the commonly encountered ones will be mentioned.

One of the unfortunate aspects of the sulfonamide drugs is the frequency with which they produce acute hemolytic anemia. Sulfanilamide is the most frequent cause of hemolytic anemia, but all the other sulfonamides have also been incriminated. The hemolytic process has been so severe in 20 per cent of these cases that hemoglobinuria has resulted, and of the patients developing hemoglobinuria approximately 15 per cent have died.

The mechanism by which the sulfonamides produce hemolysis is not clear. Osmotic fragility

MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Stated Meeting, October 3, 1945

A STATED meeting of the Council was called to order by the president, Dr Reginald Fitz, Suffolk, on Wednesday, October 3, 1945, at 10 30 a m, in John Ware Hall, 8 Fenway, Boston The secretary, Dr Michael A Tighe, Middlesex North, served as recorder, 211 councilors (Appendix No 1) were present

In opening the meeting the President read the following obituary

It is the President's sad duty to open this meeting by reporting the death of Philemon Edwards Truesdale, a councilor from the Bristol South District and for several years a member of the Committee on Cancer He died at Fall River on June 12, in his seventy-first year

Dr Truesdale received his degree from the Harvard Medical School in 1898, soon entered practice in Fall River and became a nationally known surgeon as director and founder of the Truesdale Hospital He joined the medical corps of the United States Army in 1917 and sailed for France with the rank of captain in the Yale Mobile Hospital Unit. In October 1918, he was promoted to the rank of major On his return to the United States he was made director of surgery at Camp Devens and was honorably discharged from the Army on March 15, 1919

He became a fellow of the Massachusetts Medical Society in 1903 and was president of the Bristol South District Medical Society from 1927 to 1928 He was vice-president of the Massachusetts Medical Society from 1933 to 1935 and one of our alternate members in the House of Delegates of the American Medical Association from 1929 to 1937

Besides being a member of the Massachusetts Medical Society and of the American Medical Association, Dr Truesdale was a member of the American Association for Thoracic Surgery, the American College of Surgeons, the American Hospital Association, the American Surgical Society, the Fall River Medical Society, the International Surgical Society, the New England Cancer Society and the New England Surgical Society

Dr Truesdale is survived by his widow, three sons and four daughters

In accordance with the President's expressed wish, the Council stood in silent respect to the memory of Dr Truesdale

Dr Fitz addressed the Council as follows

Our by-laws state that the president shall preside at the meetings of the Council The rules of the Council specify that new business offered at any meeting shall be referred to an appropriate committee before any action is taken on it, and also that committee reports shall be referred to the Executive Committee for consideration before any action is taken on them

The President believes that these two rules are of great significance They are designed to prevent impetuous action by the Society's deliberative body Moreover, they create, in effect, a reference committee by which resolutions, measures and propositions to be presented to the Council by any of its committees shall first be filtered through a small and representative group of its members elected for such service by their district societies

In presiding at today's meeting, the President will invite the chairman of each committee which has expressed intention of reporting to render its report In case any chairman is not a member of the Council, the President, with the permission of the Council, will offer him the privileges of the floor After the report has been accepted, the President will present the Executive Committee's views on it and will then state the question concerned in the report as clearly as he can It then comes before the assembly for debate and action

The President reminds the Council that Robert's *Rules of Order* govern our deliberations when not in conflict with our by-laws This authority states that debate must be limited to the merits of the immediately pending question, and that no member can speak a second time to a question so long as any member desires to speak who has not spoken the question The President asks each councilor who obtains the floor to announce his name and his district society before speaking and to speak from the desk so that his remarks can be easily heard by all in attendance In addition no motion should be discussed until it is seconded

REPORTS OF COMMITTEES

Executive Committee — Dr Michael A Tighe, Middlesex North, secretary

In presenting this report (Appendix No 2) the Secretary said that the Executive Committee had met three times since it last reported to the Council The meeting held on May 23, 1945, was in lieu of the annual meeting of the Council, the wartime restrictions imposed by the Office of Defense Transportation having made this latter meeting impossible

The second meeting, he said, was of an emergency character and had to do with two items of business which were of pressing importance The first was concerned with a fee schedule (Appendix No 3) which the Society had been asked to set up by the Massachusetts Department of Education, Division of Rehabilitation He added that this schedule was submitted by the Committee on Rehabilitation — Dr Joseph H Shortell, Suffolk, chairman, — its purpose being to act as a guide in the payment for medical services rendered to those covered by the rehabilitation program He said that those coming within the scope of this program need not show indigence but must be without the means of paying for these services themselves He added that it was hoped by the rehabilitation program to restore those with remediable and static difficulties to their full economic value to the community

The Secretary said that the Executive Committee approved this schedule in the name of the Council He noted that Dr Richard Dutton, Middlesex East, was recorded as disapproving

He moved that the Council approve this act of the Executive Committee This motion was seconded by Dr Walter G Phippen, Essex South

Dr Allan M Butler, Suffolk, was recognized by the chair He called attention to the following four charges which to him seemed unfortunate hemoglobin (Sahl), \$2 00, sedimentation rate, \$5 00, hematocrit, \$3 00, serum nonprotein nitrogen, \$3 00, and serum chloride, \$3 00 He said that he wished to emphasize the point that the last two determinations were relatively simple and that an inexperienced technician in a laboratory could carry out

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The President said that the report contained one recommendation that had to do with the time and place of the annual meeting. He added that this recommendation had been approved by the Executive Committee. It was regularly moved and seconded that the recommendation be adopted, and it was so ordered by vote of the Council.

Committee on Legislation — Dr William E. Browne, Suffolk, chairman

This report (Appendix No. 4) was offered by the chairman as published in the circular of advance information. It reviewed the work of the committee during the 1945 legislative session. It said that the committee had acted upon nineteen bills in the Senate and fifty-one bills in the House. It recorded the resignation of Dr. Browne as chairman and the election of Dr. Humphrey L. McCarthy, Norfolk, in his place.

It paid tribute to the efforts of Dr. H. Quimby Gallupe, secretary of the State Board of Registration in Medicine, to Dr. Vlado A. Getting, Commissioner of Public Health, to the officers of the Society, to the efforts of certain district societies, noting that, in some of these, action had been feeble, and, finally, to certain members of the Senate and House.

This report also included Governor Tobin's message that accompanied his veto of the Chiropractic Bill.

It was moved by Dr. Browne and seconded by Dr. Hornor that the report be accepted. It was so ordered by vote of the Council.

The President noted that this report contained the following recommendation:

That a column be printed from time to time, as indicated, in the *New England Journal of Medicine* which shall be devoted to legislative affairs and which shall be prepared by the chairman of the Committee on Legislation.

It was moved and seconded that this recommendation be adopted, and it was so ordered by vote of the Council. (Dr. Browne left the platform amid applause.)

Committee on Public Relations — Dr. Albert A. Hornor, Suffolk, secretary

This report, which is as follows, was offered by Dr. Hornor:

The Committee on Public Relations of the Massachusetts Medical Society met on August 1 at the Harvard Club, at this meeting there were present ten members of the committee. There was no action taken which will require confirmation or approval by the Executive Committee.

Progress reports were made by several committees. A report of the Subcommittee on Public Information was made by Dr. John Fallon. Dr. Daniel Reardon reported on the Subcommittee on Labor and Industry. Dr. Howard F. Root made a report on the Committee on Postwar Planning and on the Subcommittee on Postgraduate Education. Dr. William E. Browne made an informal report on the Committee on Legislation. Dr. Hornor, in the absence

of Dr. John Dumphy, made a report on the Subcommittee on Tax-Supported Medical Care.

Dr. Hornor moved the acceptance of the report. This motion was seconded by Dr. Phippen, and it was so ordered by vote of the Council.

Subcommittee on Labor and Industry — Dr. Daniel B. Reardon, Norfolk South, chairman

This report, which is as follows, was offered by Dr. Reardon:

During the past year, your committee has had three meetings, two with representatives of the two major groups of organized labor, and one meeting with members of the Associated Industries of Massachusetts. At all these meetings the important question which was discussed was medical-care costs to the working man and what means should be established to meet these costs.

Although the discussion at these meetings consumed about two hours, your committee was informed that labor has definite ideas as to how this cost should be met, and also that the representatives of industry have some ideas about this same question. The important facts brought out at these meetings are as follows:

- 1 The CIO representatives expressed themselves in favor of "adequate medical care at the price the worker is able to pay."

- 2 The A. F. of L. representatives stated that in their opinion the demand should be met by an insurance plan, the entire cost of which should be borne by industry.

- 3 The representatives of industry stated that it was their opinion that the entire cost of medical care could not be borne by industry at this time, because it would place an additional cost on production, thus making their production costs higher than their competitors in other states, who did not have the same coverage. They also brought to the front two phases of the problem, namely, medical-care costs, and loss of income to the employee during illness. Although they stated that they had no definite answer as yet to the medical-care costs, they felt that the question of loss of income during illness was a social and economic problem and should probably best be provided by state or national legislation.

Both industry and labor representatives did not endorse any scheme such as compulsory health insurance. Labor objected on the grounds that it would mean an additional contribution from labor to pay the costs, and industry objected to such legislation because it would mean state or national medical supervision.

Since we have held our meetings, it has been brought to our attention that some industrial concerns have adopted a comprehensive insurance plan with extensive coverage for their employees. Whether or not this plan will be taken up by other industries, we cannot state at the present time.

In exploring this field, your committee believes that it has obtained the opinions of labor and industry relative to medical-care costs as expressed by them in good faith. This is only a beginning, future conferences may solve the answer to this perplexing problem.

Dr. Reardon moved the acceptance of the report. This motion was seconded by Dr. Guy L. Richardson, Essex North, and it was so ordered by vote of the Council.

Other Standing Committees

The President announced that, although the following standing committees had reported during the year as provided for in the by-laws, they offered no reports on this occasion: Ethics and Discipline, Industrial Health, Medical Defense,

forty of them a day Dr George L Schadt, Hampden, asked Dr Butler if he considered the fees in this schedule too high Dr Butler responded that he did not so consider all of them Dr Schadt said that Dr Butler's claim might be so as it related to the larger laboratories but that it was not so in the smaller private laboratories He expressed the thought that on the whole the fees for laboratory work as set forth in the schedule were adequate and equitable

The motion was carried by vote of the Council

The Secretary said that the second item of business considered at this emergency meeting of the Executive Committee had to do with a request which came from the Society's delegates to the Council of the State Medical Societies of New England that \$100 be contributed by the Society toward defraying the expenses of this council He said that the Executive Committee approved of this request He moved that the Council approve this act of the Executive Committee This motion was seconded by Dr Allen G Rice, Hampden, and it was so ordered by vote of the Council

The Secretary said that the third or pre-Council meeting of the Executive Committee was held on September 26, 1945, and that the committee reviewed all the committee reports that appeared on the agenda being considered by the Council He said that the committee recommended that the reports that were purely informational be accepted and that, in the case of those that contained recommendations, the recommendations be adopted with one exception, namely, that, in the case of the report of the Committee Appointed to Study a Possible Revision of the By-laws as They Relate to the Election of Fellows, the Executive Committee recommended that the words "if possible" appearing in Recommendation No 2 be deleted and that the word "may" be inserted between the word committee and the word "be" appearing in the same recommendation He said that action on this recommendation would be sought when the report of this committee was before the Council for action

The Secretary said that the Executive Committee noted the withdrawal of the report of the Subcommittee on Public Information and likewise the withdrawal of Recommendations No 1 and 2, which appeared in the supplementary report of the Committee on Postwar Planning He said that the Executive Committee approved a resolution submitted jointly by the Committee on Public Relations, Committee on Legislation and Committee on Postwar Planning He added that this resolution represented an attempt to meet in the person of one individual the needs of the Society as seen by these committees This resolution, he continued, would be formally before the Council later in the meeting

The Secretary said that the Executive Committee had approved of the President's act in appointing two fellows of the Society to attend, at

the Society's expense, a conference on public relations in Chicago, which was to be held under the auspices of the Council on Medical Service and Public Relations of the American Medical Association He moved that the Council do likewise This motion was seconded by a councilor, and it was so ordered by vote of the Council

The Secretary read a list (Appendix No 2) of ad interim appointments made by the President. He said that the Executive Committee had approved these appointments and moved that the Council do likewise This motion was seconded by Dr Albert A Hornor, Suffolk, and it was so ordered by vote of the Council

He spoke of a communication that had been received from the Committee on Rural Medical Service of the American Medical Association and said that when this communication was formally before the Council the committee would recommend that the President be directed to appoint a committee of three to confer with a committee of the Massachusetts Farm Bureau Federation concerning rural medical service

The Secretary moved the adoption of the report as a whole This motion was seconded by Dr William M Collins, Middlesex North, and it was so ordered by vote of the Council

Committee on Finance — Dr Francis C Hall, Suffolk, chairman

Dr Hall reported as follows

The only things that the Finance Committee has done since the last report are to approve the budget of \$1000 for a Committee on Public Information, under Dr Fallon, and to approve the activation of a postwar loan fund, which called for no appropriation

Dr David Cheever, Suffolk, moved the acceptance of the report This motion was seconded by Dr Leroy E Parkins, Suffolk, and it was so ordered by vote of the Council

The President said that this report contained two recommendations one that had to do with confirming the committee's action in approving an appropriation of \$1000 for the Subcommittee on Public Information and the other its action in approving the activation of a postwar loan fund

Dr Phippen moved their acceptance This motion was seconded by Dr Rice and it was so ordered by vote of the Council

Committee on Arrangements — Dr Roy J Heffernan, Norfolk, chairman

The report, which is as follows, was offered by the chairman

A meeting of the committee was held on August 29 It is recommended that the annual meeting be held in Boston on May 21, 22 and 23, 1946 Space has been reserved at the Hotel Statler for these dates

Dr Heffernan moved the acceptance of the report This motion was seconded by Dr Peirce H Leavitt, Plymouth, and it was so ordered by vote of the Council

attending small-loan banking Dr Reardon also asked for this information Dr Schadt took the question and answered as follows

The committee appointed by the President, consisting of Dr Hubbard, the treasurer, Dr Tighe, the secretary, Dr Parkhurst, Dr Lund and myself have had many meetings. We studied this whole problem, and then we had a meeting with Mr Wallace, State Commissioner of Banking. Mr Wallace brought to our attention in our first meeting the difficulties that would arise as a result of Schedule W, as promulgated by the Government with reference to borrowing money for certain equipment, and Mr Wallace was very strongly of the opinion that the better way of running this fund was to do it through a commercial bank, using the \$25,000 of the Society, in bonds or stocks as collateral against the money that would be borrowed by the members of the Society.

He pointed out that it would cost 5 per cent, that there would be certain work that the bank would have to do, which would be covered by the 5 per cent, and that we could stick to the 2 per cent if we wished, paying the difference to the bank, or that later, when the committee talked it over, we could ask the returning veteran to pay the whole 5 per cent.

In a later meeting the committee unanimously agreed that the better plan would be to stick to the 2 per cent that we were going to charge our returning members and that the Society should pay the difference.

Just remember that the \$25,000 that the Society has allocated to this work is in bonds and stocks, and will be kept that way. The bonds will simply be put up as collateral. We still get interest on those bonds at 2½ per cent, amounting to \$750. When the receipt of this interest is taken into consideration it will be found that the Society's income, by reason of this loan, will suffer to the extent of \$125.

Dr Hubbard said in response to a question by Dr James C McCann, Worcester, that the amount borrowed could be up to \$25,000, the amount represented by the collateral put up by the Society. He added that a total of fifty loans of \$500 each would thus be available. He also said that, if the Society assumed the payment of 3 of the 5 per cent to be charged on these loans, as proposed in this plan, the Society would escape practically all administrative expense and that probably it would be found that one would balance the other.

In answer to a question by Dr Richardson, Dr Schadt said that the Society guaranteed both the principal and interest. Dr Richardson asked if the Society could not simply issue a note to the bank in the sum of \$25,000 without putting up collateral. Dr Hubbard said that the collateral is required.

Dr Walter H Pulsifer, Plymouth, asked if the total number of \$500 loans available under this fund would be 50. Dr Schadt replied in the affirmative.

Dr Harold G Giddings, Middlesex South, asked how long the loans would run, whether they could be renewed and what was the limit in amount of the individual loan. Dr Schadt said that the limit was \$500 per loan, that it was payable in a year and that it might be renewed. He added that further extension of the amount of the fund was a subject for future decision by the Council.

In response to a question by Dr Leavitt, Dr Hubbard said he was sure he could obtain the money at a total rate of 5 per cent.

Dr Rice asked if the individual loan was discounted at the start. Dr Hubbard replied in the affirmative.

The motion as amended was adopted by vote of the Council.

Dr Edward P Bagg, Hampden, moved the adoption of the first recommendation, which would rescind the action of the Executive Committee of May 23, 1945, concerning the administration of this fund. This motion was seconded by Dr Phippen, and it was so ordered by vote of the Council.

The report as a whole, as amended, was adopted by vote of the Council.

Committee on Postwar Planning — Dr Howard F Root, Suffolk, chairman.

This report (Appendix No 5) was offered by Dr Root. In offering the report Dr Root spoke as follows:

This week the *Journal of the American Medical Association* has provided the present new up-to-date list of residencies now available throughout the United States. Many of you have probably seen this, the figures are rather striking.

In Massachusetts there are 80, of which nearly all are provided by a very small number of institutions. New York City, with 115, is providing the largest number of residencies and fellowships. Boston is next, and Chicago has 65. But the fact is that the Commonwealth of Massachusetts is really indebted to a very small number of institutions for the provision of this number of opportunities, and certainly this report, which will interest everyone, indicates the need for us to do more rather than less.

Dr Root moved the acceptance of the report. This motion was seconded by Dr Rice, and it was so ordered by vote of the Council.

A supplementary report of his committee was offered by Dr Root as follows:

The Committee on Postwar Planning recommends: (1) That the Council approve the appointment of a full-time director of medical education who shall be a physician. (2) That the Council authorize the President to appoint a committee to secure such a director of medical education. (3) That the Council approve a supplementary budget for the use of the Subcommittee on Postgraduate Education for the balance of 1945 as follows: Clinical Information Bureau and office expense and wages, \$1000, and for payment of instructors and incidental expenses in providing postgraduate instruction in ten or twelve localities this fall, \$1500, a total of \$2500.

Dr Root announced that the first and second recommendations had been withdrawn by his committee. He moved the adoption of the third recommendation. This motion was seconded by Dr Phippen. The Secretary announced that the Committee on Finance had approved the expenditure called for in this recommendation.

Dr Schadt said:

I had the impression that most of this course, or much of it, was to be given by the Government or by the State Department of Public Health and that considerable, if not all, of the expense was to be borne by them. I am rather surprised to hear that the Society is now asked to add \$1500 to the budget of this committee for the payment of instructors. I thought that the Government and

Medical Education, Publications, Public Health and Society Headquarters. He likewise announced that the Committee on Membership had reported to the Executive Committee on those matters which according to the by-laws have their final action in the latter committee. He added that the Committee on Membership had no additional report. On a motion by Dr. Richard M. Smith, Suffolk, and a second by Dr. Leavitt, it was voted to accept a report of "no report" from the above-mentioned committees.

Committee on Postwar Loan Fund—Dr. George Leonard Schadt, Hampden, chairman

Dr. Schadt offered the following report:

Your committee has had several fully attended meetings, and has discussed in considerable detail the plan to be followed in activating the work of the committee. Dr. Eliot Hubbard, Jr., treasurer of the Society and a member of the committee, and Mr. Robert St. B. Boyd, executive secretary, have, at the request of the committee, had many conferences with a number of commercial and federal-reserve bank officials, and Dr. Tighe, Dr. Hubbard, Mr. Boyd and your chairman have had a most interesting and valuable conference with Mr. Wallace, State Commissioner of Banking.

As a result of these various conferences and after considerable discussion, the committee wishes to report as follows:

It is the opinion of the Committee on Postwar Loan Fund that the proper way to handle loans under the fund is through the instrumentality of a commercial bank, the contribution of the Massachusetts Medical Society being the guaranteeing of the loan and the absorption of the difference in interest between the amount actually charged for the borrowed money and the 2 per cent paid by the member borrowing under this loan.

This opinion was arrived at unanimously, since it became evident to the committee that there were many complicated elements entering into making loans of this kind and that these complications were largely the result of Government regulations and restrictions. This made the business at hand a strictly banking procedure, and because we did not possess in our organization the skills required, it was thought wise to turn the actual business details of such loans over to a bank. The committee, in submitting this report, recommends:

That it be permitted to activate the work of the Committee on Postwar Loan Fund within the framework as outlined above, rather than as voted by the Executive Committee acting for the Council at the meeting in May, at which time the committee was authorized to function on the premise that only 2 per cent or less should be paid by the member borrowing under the loan. The present plan retains this feature, namely, that the member shall pay only 2 per cent, the added interest being assumed by the Massachusetts Medical Society.

Dr. Schadt moved the acceptance of the report. This motion was seconded by Dr. Phippen.

Dr. Cheever inquired how many returned veterans had sought the assistance of the Massachusetts Medical Society. Dr. Schadt replied, "Ten." He explained the small number by saying that no publicity could be given to this matter until the Council had taken action on it.

The motion was adopted by vote of the Council.

The President pointed out that this report contained two recommendations. First, that the action of the Executive Committee on May 23, 1945,

in approving that part of the report of the Committee on Postwar Loan Fund that had to do with certain administrative details be rescinded and, secondly, that the fund created under this auspice be administered through a loan from such commercial bank or banks as the committee, with the approval of the Treasurer, may select, the Society guaranteeing the principal of the loan and absorbing the difference in the interest charged by the bank or banks and the 2 per cent that will be paid by the individual borrower.

At the suggestion of Dr. Donald Munro, Suffolk, the President called for action on the second recommendation. A motion to adopt this recommendation was offered by Dr. Edward P. Bagg, Hampden. This motion was seconded by Dr. Phippen.

Dr. Munro pointed out that as the administrative detail is set up in this recommendation there is no limit set concerning the total amount of interest that will be charged by the bank in any particular loan. He expressed it as his opinion that such limits should be set forth in the recommendation itself.

Dr. Eliot Hubbard, Jr., treasurer, explained that, although it was true that a limit for the total interest rate that the banks might charge was not set forth in the recommendation, an agreement had already been reached with a bank whereby this total rate would be 5 per cent—the individual obtaining the loan paying 2 per cent, and the Society 3 per cent.

Dr. Munro, in reiterating his belief that the limits as set forth by Dr. Hubbard should be incorporated in the recommendation, moved to amend the recommendation by adding to the next to the last line the words "not to exceed 3 per cent." In its amended form, he said, this last sentence of this recommendation would read as follows:

The present plan retains this feature, namely, that the member shall pay only 2 per cent, the added interest, not to exceed 3 per cent, being assumed by the Massachusetts Medical Society.

This amendment was seconded by a councilor.

Dr. Schadt expressed himself as being in accord with the amendment. It was apparently also agreeable to the maker of the motion and its seconder.

Dr. Parkins inquired how long the postwar loan fund would be available, and Dr. Reardon asked the Treasurer to clarify the question of loans and the Society's ability to pay them, saying that the latter had given information of this character to the Executive Committee. Dr. Hubbard responded as follows:

The Society takes the \$25,000 that has been authorized to work with and puts it up as collateral with the commercial bank. The commercial bank makes loans to the applying member. The commercial bank will charge 5 per cent for this service. Therefore, the Society will have to take on 3 per cent of that charge in the plan as outlined here.

Dr. William F. Ryan, Middlesex North, suggested that the Treasurer tell the Council of the difficulties

attending small-loan banking Dr Reardon also asked for this information Dr Schadt took the question and answered as follows

The committee appointed by the President, consisting of Dr Hubbard, the treasurer, Dr Tighe, the secretary, Dr Parkhurst, Dr Lund and myself have had many meetings We studied this whole problem, and then we had a meeting with Mr Wallace, State Commissioner of Banking Mr Wallace brought to our attention in our first meeting the difficulties that would arise as a result of Schedule W, as promulgated by the Government with reference to borrowing moneys for certain equipment, and Mr Wallace was very strongly of the opinion that the better way of running this fund was to do it through a commercial bank, using the \$25,000 of the Society, in bonds or stocks as collateral against the money that would be borrowed by the members of the Society

He pointed out that it would cost 5 per cent, that there would be certain work that the bank would have to do, which would be covered by the 5 per cent, and that we could stick to the 2 per cent if we wished, paying the difference to the bank, or that later, when the committee talked it over, we could ask the returning veteran to pay the whole 5 per cent.

In a later meeting the committee unanimously agreed that the better plan would be to stick to the 2 per cent that we were going to charge our returning members and that the Society should pay the difference

Just remember that the \$25,000 that the Society has allocated to this work is in bonds and stocks, and will be kept that way The bonds will simply be put up as collateral We still get interest on those bonds at $2\frac{1}{2}$ per cent, amounting to \$750 When the receipt of this interest is taken into consideration it will be found that the Society's income, by reason of this loan, will suffer to the extent of \$125

Dr Hubbard said in response to a question by Dr James C McCann, Worcester, that the amount borrowed could be up to \$25,000, the amount represented by the collateral put up by the Society He added that a total of fifty loans of \$500 each would thus be available He also said that, if the Society assumed the payment of 3 of the 5 per cent to be charged on these loans, as proposed in this plan, the Society would escape practically all administrative expense and that probably it would be found that one would balance the other

In answer to a question by Dr Richardson, Dr Schadt said that the Society guaranteed both the principal and interest Dr Richardson asked if the Society could not simply issue a note to the bank in the sum of \$25,000 without putting up collateral Dr Hubbard said that the collateral is required

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In response to a question by Dr Leavitt, Dr Hubbard said he was sure he could obtain the money at a total rate of 5 per cent

Dr Rice asked if the individual loan was discounted at the start Dr Hubbard replied in the affirmative

The motion as amended was adopted by vote of the Council

Dr Edward P Bagg, Hampden, moved the adoption of the first recommendation, which would rescind the action of the Executive Committee of May 23, 1945, concerning the administration of this fund This motion was seconded by Dr Phippen, and it was so ordered by vote of the Council

The report as a whole, as amended, was adopted by vote of the Council

Committee on Postwar Planning — Dr Howard F Root, Suffolk, chairman

This report (Appendix No 5) was offered by Dr Root In offering the report Dr Root spoke as follows

This week the *Journal of the American Medical Association* has provided the present new up-to-date list of residencies now available throughout the United States Many of you have probably seen this, the figures are rather striking

In Massachusetts there are 80, of which nearly all are provided by a very small number of institutions New York City, with 115, is providing the largest number of residencies and fellowships Boston is next, and Chicago has 65 But the fact is that the Commonwealth of Massachusetts is really indebted to a very small number of institutions for the provision of this number of opportunities and certainly this report, which will interest everyone, indicates the need for us to do more rather than less

Dr Root moved the acceptance of the report This motion was seconded by Dr Rice, and it was so ordered by vote of the Council

A supplementary report of his committee was offered by Dr Root as follows

The Committee on Postwar Planning recommends (1) That the Council approve the appointment of a full-time director of medical education who shall be a physician (2) That the Council authorize the President to appoint a committee to secure such a director of medical education (3) That the Council approve a supplementary budget for the use of the Subcommittee on Postgraduate Education for the balance of 1945 as follows: Clinical Information Bureau and office expense and wages, \$1000, and for payment of instructors and incidental expenses in providing postgraduate instruction in ten or twelve localities this fall, \$1500, a total of \$2500

Dr Root announced that the first and second recommendations had been withdrawn by his committee He moved the adoption of the third recommendation This motion was seconded by Dr Phippen The Secretary announced that the Committee on Finance had approved the expenditure called for in this recommendation

Dr Schadt said

I had the impression that most of this course, or much of it, was to be given by the Government or by the State Department of Public Health and that considerable, if not all, of the expense was to be borne by them I am rather surprised to hear that the Society is now asked to add \$1500 to the budget of this committee for the payment of instructors I thought that the Government and

Medical Education, Publications, Public Health and Society Headquarters. He likewise announced that the Committee on Membership had reported to the Executive Committee on those matters which according to the by-laws have their final action in the latter committee. He added that the Committee on Membership had no additional report. On a motion by Dr. Richard M. Smith, Suffolk, and a second by Dr. Leavitt, it was voted to accept a report of "no report" from the above-mentioned committees.

Committee on Postwar Loan Fund—Dr. George Leonard Schadt, Hampden, chairman.

Dr. Schadt offered the following report:

Your committee has had several fully attended meetings, and has discussed in considerable detail the plan to be followed in activating the work of the committee. Dr. Eliot Hubbard, Jr., treasurer of the Society and a member of the committee, and Mr. Robert St. B. Boyd, executive secretary, have, at the request of the committee, had many conferences with a number of commercial and federal-reserve bank officials, and Dr. Tighe, Dr. Hubbard, Mr. Boyd and your chairman have had a most interesting and valuable conference with Mr. Wallace, State Commissioner of Banking.

As a result of these various conferences and after considerable discussion, the committee wishes to report as follows:

It is the opinion of the Committee on Postwar Loan Fund that the proper way to handle loans under the fund is through the instrumentality of a commercial bank, the contribution of the Massachusetts Medical Society being the guaranteeing of the loan and the absorption of the difference in interest between the amount actually charged for the borrowed money and the 2 per cent paid by the member borrowing under this loan.

This opinion was arrived at unanimously, since it became evident to the committee that there were many complicated elements entering into making loans of this kind and that these complications were largely the result of Government regulations and restrictions. This made the business at hand a strictly banking procedure, and because we did not possess in our organization the skills required, it was thought wise to turn the actual business details of such loans over to a bank. The committee, in submitting this report, recommends:

That it be permitted to activate the work of the Committee on Postwar Loan Fund within the framework as outlined above, rather than as voted by the Executive Committee acting for the Council at the meeting in May, at which time the committee was authorized to function on the premise that only 2 per cent or less should be paid by the member borrowing under the loan. The present plan retains this feature, namely, that the member shall pay only 2 per cent, the added interest being assumed by the Massachusetts Medical Society.

Dr. Schadt moved the acceptance of the report. This motion was seconded by Dr. Phippen.

Dr. Cheever inquired how many returned veterans had sought the assistance of the Massachusetts Medical Society. Dr. Schadt replied, "Ten." He explained the small number by saying that no publicity could be given to this matter until the Council had taken action on it.

The motion was adopted by vote of the Council.

The President pointed out that this report contained two recommendations. First, that the action of the Executive Committee on May 23, 1945,

in approving that part of the report of the Committee on Postwar Loan Fund that had to do with certain administrative details be rescinded and, secondly, that the fund created under this auspice be administered through a loan from such commercial bank or banks as the committee, with the approval of the Treasurer, may select, the Society guaranteeing the principal of the loan and absorbing the difference in the interest charged by the bank or banks and the 2 per cent that will be paid by the individual borrower.

At the suggestion of Dr. Donald Munro, Suffolk, the President called for action on the second recommendation. A motion to adopt this recommendation was offered by Dr. Edward P. Bagg, Hampden. This motion was seconded by Dr. Phippen.

Dr. Munro pointed out that as the administrative detail is set up in this recommendation there is no limit set concerning the total amount of interest that will be charged by the bank in any particular loan. He expressed it as his opinion that such limits should be set forth in the recommendation itself.

Dr. Eliot Hubbard, Jr., treasurer, explained that, although it was true that a limit for the total interest rate that the banks might charge was not set forth in the recommendation, an agreement had already been reached with a bank whereby this total rate would be 5 per cent—the individual obtaining the loan paying 2 per cent, and the Society 3 per cent.

Dr. Munro, in reiterating his belief that the limits as set forth by Dr. Hubbard should be incorporated in the recommendation, moved to amend the recommendation by adding to the next to the last line the words "not to exceed 3 per cent." In its amended form, he said, this last sentence of this recommendation would read as follows:

The present plan retains this feature, namely, that the member shall pay only 2 per cent, the added interest, not to exceed 3 per cent, being assumed by the Massachusetts Medical Society.

This amendment was seconded by a councilor.

Dr. Schadt expressed himself as being in accord with the amendment. It was apparently also agreeable to the maker of the motion and its seconder.

Dr. Parkins inquired how long the postwar loan fund would be available, and Dr. Reardon asked the Treasurer to clarify the question of loans and the Society's ability to pay them, saying that the latter had given information of this character to the Executive Committee. Dr. Hubbard responded as follows:

The Society takes the \$25,000 that has been authorized to work with and puts it up as collateral with the commercial bank. The commercial bank makes loans to the applying member. The commercial bank will charge 5 per cent for this service. Therefore, the Society will have to take on 3 per cent of that charge in the plan as outlined here.

Dr. William F. Ryan, Middlesex North, suggested that the Treasurer tell the Council of the difficulties

intended to pay the person selected an honorarium equal to the full-time salaries paid to physicians in Massachusetts who occupy most responsible positions. He presumed that this would mean anywhere from \$10,000 to \$15,000 per year. He added that these were large sums and that the need and usefulness of such a step must be clearly defined. He said that he thoroughly agreed with Dr. Fallon concerning the need of a competent person to guide the Society in its public approach. He added, however, that there were too many generalities in the preamble that ought to be defined. He asked what was meant by the following: "The task entailed in organizing and activating means to make the various educational facilities of the Society of the greatest possible value to physicians and the public at large." In this connection he asked what were the facilities of the Massachusetts Medical Society. He said that he regarded these facilities as being represented by the brains of the various members of the Society. He urged support of the Boston Medical Library. Finally, he cautioned the members to proceed slowly before committing themselves to the expenditure of the very considerable sum involved.

Dr. Elmer S. Bagnall, Essex North, said that this subject had been under discussion for fifteen years. He expressed himself as believing that anyone who has presided over the destinies of the Society soon becomes aware of the necessity of having a full-time officer who could focus the thinking and functions of the Society in the interest of the community and of the profession at large. He pointed out that, by comparison with certain other states, the dues of \$10.00 per year were small and that, if it is necessary, they could be increased. He thought that the proper person could be found for the job.

Dr. Phippen said that he would like to speak on the issue raised by Dr. Cheever. He said that he was very much interested in utilizing the educational possibilities of the small hospitals of the state. He pointed out that, outside certain teaching centers, there were extremely few hospitals equipped to handle residencies. A person trained in this work, he added, could supply the inspiration and help necessary to make realities out of these possibilities. In expressing agreement with Dr. Cheever that there should be a more widespread use of the Boston Medical Library, he said that such a director would be in a splendid position to bring home to the small hospital and its staff the value of the library. He expressed the hope that the resolution would prevail.

At that point the Council went into executive session.

The Council rose out of executive session at 1:15 p.m.

At the request of the President, the Secretary reread the joint resolution whose adoption had

been moved and seconded before the Council went into executive session.

Dr. Hornor moved, as an amendment, the adoption of the resolution provided that the following sentence be added to it: "Such a director of medical information and education shall be appointed by the Council on proposal by a committee of seven named by the President." This amendment was seconded by Dr. Root. (The amendment put into the resolution a provision specified in the preamble.) The amendment was adopted by vote of the Council.

Dr. Fallon moved the adoption of the resolution as amended. This motion was seconded by Dr. Leavitt, and it was so ordered by vote of the Council.

Committee Appointed to Study a Possible Revision of the By-laws as They Relate to the Election of Fellows — Dr. Charles J. Kickham, Norfolk, chairman.

This report (Appendix No. 6) was offered by Dr. Kickham, who referred to the report as printed in the circular of advance information.

He said that the Executive Committee recommended that the words "if possible" as appearing in the second recommendation be deleted and that the word "may" be inserted between the word "committee" and the word "be," likewise as appearing in the second recommendation.

He moved the acceptance of the report subject to these changes. This motion was seconded by Dr. Phippen, and it was so ordered by vote of the Council.

The adoption of the recommendations contained in the report, subject to the changes noted by Dr. Kickham, was moved by Dr. Leavitt. This motion was seconded by Dr. Richardson. The recommendations as amended are as follows:

- (1) That letters recommending candidates from non-approved or foreign medical schools be definitely detailed, specific and informative in regard to the applicant.
- (2) That an officer of the district society or a member of the district membership committee may be present at the deliberations of the State Committee on Membership when applicants from their district are under consideration.
- (3) That the State Committee on Membership, acting within the by-laws, invite an officer of the district society or a member of the district committee on membership to review with them the record of an applicant before final decision of disapproval of such an applicant is made.

Their adoption was ordered by vote of the Council.

Dr. Kickham moved the adoption of the report as a whole as amended. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Medical Advisory Committee to Regional OPA — Dr. Joseph Garland, Suffolk, chairman.

This report, which is as follows, was offered by the Secretary in the absence of Dr. Garland.

Certain changes have taken place in food rationing, which, it is hoped, will expedite the work of your com-

the State Department of Public Health, in putting on their program of child welfare and maternity work, were to furnish the instructors and pay them Am I mistaken?

Dr Root replied that Dr Schadt was mistaken in his assumption and that, although it was true that the Commonwealth would contribute to the program, it would not finance it in its entirety. In reply to a further question by Dr Schadt, Dr Root said that he did not know how much the state contribution would be. He referred Dr Schadt to Dr Ohler, chairman of the subcommittee having this work in hand.

The motion to adopt the recommendation was passed by vote of the Council.

Committee on Public Relations, Committee on Legislation and Committee on Postwar Planning

At the direction of the President, the Secretary read a joint report and resolution offered by these committees as follows:

There is need for the Massachusetts Medical Society to express to a wide audience its opinion on matters of public health. Better relations between the public and the Society than now exist are urgently needed. Our experience in postgraduate medical education, information and legislation has already made it plain that we can be of greater use to our members and the public than heretofore.

We believe that the Society, as a vehicle of education, is under an obligation to offer its opinion on medical affairs to the public in an honest, intelligent and ethical manner.

The task entailed in organizing and activating means to make the various educational facilities of the Society of greatest possible value to physicians and the public is large. We recommend that a new position in the Society be created—that of Director of Medical Information and Education. The incumbent should, if possible, be a physician well enough known by the members at large so as to have their confidence, he should have sufficient energy, zeal and imagination to be able to develop the duties of such a post successfully.

Since the position would be of major importance to the welfare of the Society, the incumbent should be appointed by the Council on proposal by a committee of seven named by the President.

The by-laws state that the Council shall vote the salaries of its employees, the level of such a director's salary, therefore, would be a matter for Council decision. In order to attract a physician to this post, we suggest that the honorarium offered must be in line with full-time salaries paid to physicians in Massachusetts who occupy our most responsible positions in medical education and administration. No candidate who promised success in this post could be attracted to it on any other basis. We therefore present the following resolution:

RESOLUTION

WHEREAS, We consider that the Massachusetts Medical Society is under obligation to make its educational facilities of increasing usefulness to fellows, to all licensed physicians in Massachusetts and to the public, therefore, be it

RESOLVED, That the Massachusetts Medical Society hereby creates a new position, its holder to be known as the Director of Medical Information and Education, charged with the duty of promoting in an ethical manner the educational usefulness of the Society to its fellows, to all licensed physicians in Massachusetts and to the public, and also charged with the performance of such other duties as the Society or the Council may require.

Dr John Fallon, Worcester, moved the acceptance of this report. This motion was seconded by Dr

Phippen, and it was so ordered by vote of the Council.

The President announced that the resolution provided that the Massachusetts Medical Society should create a new position, its holder to be known as the Director of Medical Information and Education and charged with the duties specified in the resolution.

Dr Fallon moved the adoption of the resolution. This motion was seconded by Dr Leavitt.

Dr Fallon said that it had become increasingly apparent to those in intimate contact with the Society's affairs that the handling of its approach to the public was being inefficiently done. He added that this was a specialized field which required specialized training, a type of training that the busy practitioner usually did not possess and had little interest in possessing. "All of us believe," continued Dr Fallon, "that this man, preferably a doctor, should have a full-time job here at headquarters. He would be the fellow who would have time to sit down and study all day and tell the rest of us what we need to know of newly proposed matters having to do with the health of the people."

Dr William A. R. Chapin, Hampden, urged speedy action on this matter.

Dr Charles J. Kickham, Norfolk, thought that the Society should proceed with caution and deliberation. He believed that the committee appointed under this resolution should not be rushed and that it should have plenty of time to canvass for the proper incumbent. He expressed some uncertainty about the medical-education phase of this resolution, adding that the Society had a comparatively limited educational program. He said that it was his conception that this new position represented a means of getting the Society's ideas concerning health matters over to the public and to those in the service of the public. Dr Kickham offered two suggestions to the committee, if and when it was appointed under this resolution: first, that the committee submit not one name but several with the candidates' respective qualifications fully set forth, and secondly, that the person finally selected perform his duties under the direction of the Secretary. He stressed this point particularly in the event that a layman was chosen.

Dr Root said that he thought that the members of the Society would want a man in this position who was interested not only in the education of the public but likewise in the scientific education of the members. He thought that it would not be too difficult to obtain a physician for the job and that the job itself would offer a real opportunity to a physician with ability along these lines. This man, he continued, would do a public-relations job and would find himself in a position where his imagination and usefulness could be great.

Dr Cheever referred to the largeness of the order involved in the proposed action. He pointed out that the preamble to the resolution said that it was

man, and Arthur W. Carr, Plymouth. There were no nominations from the floor. Dr. Richardson moved that the Secretary be instructed to cast one ballot bearing the names of the above-named nominees. This motion was seconded, and it was so ordered by vote of the Council.

The Secretary announced that he had complied with the directive and the President declared the nominations confirmed.

NEW BUSINESS

Communications

At the direction of the President the Secretary read the following letter

Dr. Michael A. Tighe, Secretary
Massachusetts Medical Society
Boston, Massachusetts
Dear Doctor Tighe:

August 28 1945

The Board of Trustees of the American Medical Association has appointed a committee to be known as the Committee on Rural Medical Service.

On invitation of the American Farm Bureau Federation, that committee has participated in a conference with representatives of the Farm Bureau Federation and has been invited to confer with a larger group composed of representatives of several national farm organizations that probably will meet during the month of September.

At the conference held in July with representatives of the American Farm Bureau Federation, the broad outline of the farm bureau plan to promote better rural health was fully discussed. It seemed to be apparent that the Farm Bureau Federation like other influential farm groups, is opposed to compulsory federal legislation and is seeking means of accomplishing on a voluntary basis improvement and assistance of medical service for the farm population. It appeared to be the consensus that practical application of proposed plans should be on a state and county level.

The Committee on Rural Medical Service of the American Medical Association was informed that the American Farm Bureau Federation is sending a letter to its component state bureaus suggesting appointment of rural health committees to confer with similar committees representing constituent state medical associations. The Committee on Rural Medical Service agreed to communicate with the secretaries of all constituent associations and express the hope that each state association would appoint a committee on rural medical service that would be available for conferences with committees of the American Farm Bureau Federation and all other farm organizations since all planning for rural health improvement must have the benefit of the experience and advice of the organized medical profession. It is respectfully suggested that you bring this matter to the attention of the proper official body of your association at the earliest possible time.

Please advise me as to any action that may be taken with respect to the appointment of a committee on rural medical service so that results may be correlated by this committee.

(Signed) Very sincerely yours,
F. S. CROCKETT, M.D., Chairman
Committee on Rural Medical Service
American Medical Association

It was regularly moved and seconded that the Council authorize the President to appoint a committee for the purposes set forth in this letter. It was so ordered by vote of the Council.

At the direction of the President the Secretary read the following letter

September 24 1945

Dr. Reginald Fitz
319 Longwood Avenue
Boston, Massachusetts
Dear Dr. Fitz:

Mr. Cabalane has asked me to write to you stating that the Blue Cross will be very happy to work with the Massachusetts Medical Society to enable the members of the Society to form a Blue Cross group. We feel that it will be perfectly possible and very desirable to make arrangements whereby doctors who are not enrolled will have the opportunity to become Blue Cross members. Physicians who might wish to transfer from certain groups through which they now hold membership to the Massachusetts Medical Society group would be allowed to do so.

Of course, it should be understood that a satisfactory method of payment would have to be evolved, and perhaps the best way would be to have the Society bill all those who become Blue Cross members for their Blue Cross dues at the same time they are billed for their Society dues.

Perhaps the members of the Society would like to protect themselves and their families against surgical and obstetric bills through membership in the Blue Shield. If so, we could work out an arrangement similar to the one we suggest for the Blue Cross. We are aware of the courtesy privileges extended to the members of the profession, but we have had some instances where doctors have asked to be covered by Blue Shield if membership in the plan were possible.

(Signed) Sincerely yours,
E. J. CUNNINGHAM
Director of Enrollment
Massachusetts Hospital Service

Under the Council rules, the President referred this communication to the Committee on Public Relations.

At the direction of the President the Secretary read the following communication

October 1 1945

Reginald Fitz, M.D.
319 Longwood Avenue
Boston, Mass.

Dear Dr. Fitz:

We wish to employ at the Newton Hospital a doctor who has only a dental degree. For a number of years he was engaged in the practice of oral surgery in Boston, retiring before the war. Since Pearl Harbor he has put in a little over a year as a volunteer anesthetist, has earned out that work very efficiently and has met the approval of the surgeons with whom he has worked.

Our question is: Is it proper for a man possessing a dental degree to work as an anesthetist in the Newton Hospital under my supervision? We would appreciate an early answer. Thanking you I am

(Signed)

Sincerely yours

R. S. HUNT, M.D.
Anesthetist-in-Chief

Under the rules, the President referred the communication to the Committee on Ethics and Discipline.

At the direction of the President the Secretary read the following letter

September 21 1945

Dr. R. Fitz, President
Massachusetts Medical Society
8 The Fenway
Boston, Massachusetts

Dear Dr. Fitz:

The American Epilepsy League has for some years been instrumental in making it easier for people suffering with convulsive disorders to get in touch with a qualified physician for their treatment. With the great number of servicemen returning with a diagnosis of epilepsy, the Veterans Administration has turned to us for advice in suggesting men capable of handling epileptics in the rural districts of Massachusetts. At the present time our referral list for Massachusetts is limited only to specialists.

I am sure that you can understand the importance of this request and our sincere desire to fulfill it. We are turning to you as president of the Massachusetts Medical Society for advice in the best manner for compiling such a list.

As you undoubtedly know, it is not necessary that a physician be a specialist in neurology to help epileptic sufferers. There are many instances where the up-to-date knowledge of treatment is not known. The League is in a position to put interested doctors in touch with these developments.

If a personal interview with you or telephone conversation will clarify my request in any way, I shall be delighted to see you. Because of the urgency of this matter, may I ask that you give it your attention at the first possible moment?

(Signed) Sincerely yours,
ESTHER C. WALTHER, Executive Secretary
American Epilepsy League, Incorporated

Under the rules, the President referred this letter to the Committee on Public Health.

Dr. Basil E. Barton, Norfolk, acting for the Norfolk District Medical Society, offered the following resolution

RESOLVED, That the president of the Massachusetts Medical Society be requested to refer to the appropriate committee a request to investigate the fee schedule of the Massachusetts Industrial Accident Board with a view to raising fees for such as indicated.

This resolution was referred by the President, under the rules, to the Committee on Public Relations.

Dr. Charles E. Mongan, Middlesex South, offered the following resolution

WHEREAS, The question has been repeatedly asked in public and private concerning the facilities of medical education in New England; and

WHEREAS, No satisfactory scientific answer has been forthcoming, therefore be it

RESOLVED, That the Massachusetts Medical Society undertake a survey of the medical educational facilities at present available in New England.

mittee, as well as that of the OPA Regional Office, so ably managed by Miss Elizabeth Golden, the food rationing specialist of that office

Rations for service men on convalescent furloughs are now issued by five military rationing boards in New England, and the medical problems of members of the armed forces will from now on be handled by service doctors

Local rationing boards have also been authorized to approve automatically the medical applications filed by repatriated civilian prisoners of war, and by veterans discharged because of illness resulting from imprisonment

This committee has always issued extra rations according to its own views, guided by the best advice available, regardless of whether cases fell outside of the narrow list of diseases prescribed by the National Research Council, and it is a source of satisfaction that the latter has recently given an opinion that medical committees should function according to their own experience

This committee has always recognized the possible need of extra rations after hemorrhage or with anemia of any type below certain hemoglobin and red-blood-count levels, with various types of allergy, and, indeed, wherever a need could be shown to exist regardless of diagnosis. Thus, the need for extra protein in the later months of pregnancy has been demonstrated, as has also the efficacy of the Schemm diet in certain forms of heart disease

Local advisory committees are now functioning in Brookline, and, through the good offices of Dr Guy Richardson, chairman of the War Participation Committee, in Brockton, Scituate, Lawrence, Pittsfield, Springfield, New Bedford, Worcester, Holyoke, Quincy and Lowell

The work of the Regional Office continues, nevertheless, to increase. Thus, in April, 1305 cases were processed, in May, 1322, in June, 1499. Something under half of these applications seem to merit approval. Cases from outside Massachusetts increased from 17 in May to 131 in June, mostly from Vermont, which seems to prefer the advice of the Massachusetts committee to the appointment of a committee of its own

The ending of the war has produced marked changes in the food rationing program — processed foods are no longer rationed, the rationing of meats and fats has been relaxed, and there is promise of an early ending of all food rationing except that of sugar

Your committee hopes that its duties will cease within the next few weeks, in the meantime, meat, fat and sugar rationing render a continued oversight necessary

This report is offered for the information of the Council

The Secretary moved the adoption of the report. This motion was seconded by Dr Chapin, and it was so ordered by vote of the Council

War Participation Committee — Dr Guy L Richardson, Essex North, chairman

Dr Richardson submitted the following report

Since our last report, physicians' committees to assist the rationing boards in Holyoke and Quincy have been organized

The only other matter of importance was a request from the Division of Employment Security of Massachusetts to approve a certificate form for veterans' disability, and to assist them by reviewing any questionable certificate. The certificate form presented was approved, and the committee voted to review any such certificate referred to us. This is the same procedure followed in the case of doctors' certificates for change of job, handled by the War Manpower Commission

With the war over, this committee asks for its discharge.

Dr Richardson moved the acceptance of the report. This motion was seconded by Dr Collins, and it was so ordered by vote of the Council

Dr Fitz said that this report contained one recommendation, namely, that the committee be discharged. It was moved and seconded that this

recommendation be adopted and that this motion include an expression of gratitude from the Society to the members of the committee for having contributed so valuably to the war effort. It was so ordered by vote of the Council

Military Postgraduate Committee — Dr W Richard Ohler, Norfolk, chairman

Dr Ohler offered the following report

Since last February, programs have been conducted as usual. Seventy-nine meetings have been held at eighteen installations scattered through New England

Up until the present moment, no final decision has been made regarding the termination of these programs throughout the country. It is assumed, however, that programs will cease at an early date. In the meantime, your committee and also the larger committee representing all the New England states are prepared to carry on.

By way of an addition to this report Dr Ohler said that this work of postgraduate instruction will cease throughout the country in December and that it is the intention of his committee to carry on until that time

He moved the acceptance of the report. This motion was seconded by Dr Root, and it was so ordered by vote of the Council

Committee on Maternal Welfare — Dr Raymond S Titus, Norfolk, chairman

In the absence of the chairman, the Secretary read the following report

On August 23 a meeting of the Committee on Maternal Welfare was held at the Boston Medical Library. The purpose of this meeting was organization. At this meeting a report on the EMIC program by a subcommittee of the Committee on Maternal Welfare was submitted

This subcommittee wrote to the secretaries of the various districts of the Society asking for their reaction to the EMIC program. A reply was obtained from only two district secretaries. One report was favorable, and the other district society expressed its unqualified disapproval. Dr McKay, who was present at the meeting, said that more than 50 per cent of the physicians in the state had participated in this program and that the results of the obstetric care, as reflected in maternal mortality, were excellent. The EMIC program will run for another year and a half, and reports of its progress will be made to this committee. The committee voted that the chairman should get in touch with Dr Ohler relative to the refresher program. No elaborate program was deemed possible because of the continued lack of manpower due to the large number of men still in the service

The Secretary moved the acceptance of the report. This motion was seconded by Dr Chapin, and it was so ordered by vote of the Council.

Other Special Committees

Dr Leavitt moved that a report of "no report" be accepted from the following special committees: Cancer, Council Rules, Expert Testimony, To Meet with Massachusetts Hospital Association, Physical Medicine and To Recommend Blue Shield Directors. This motion was seconded by Dr Phippen, and it was so ordered by vote of the Council

APPOINTMENT OF AUDITING COMMITTEE

The following Auditing Committee was nominated by the President: William B Robbins, Suffolk, chair-

man, and Arthur W Carr, Plymouth There were no nominations from the floor Dr Richardson moved that the Secretary be instructed to cast one ballot bearing the names of the above-named nominees This motion was seconded, and it was so ordered by vote of the Council

The Secretary announced that he had complied with the directive and the President declared the nominations confirmed

NEW BUSINESS

Communications

At the direction of the President the Secretary read the following letter.

August 28 1945

Dr Michael A Tighe, Secretary
Massachusetts Medical Society
Boston, Massachusetts
Dear Doctor Tighe

The Board of Trustees of the American Medical Association has appointed a committee to be known as the Committee on Rural Medical Service.

On invitation of the American Farm Bureau Federation, that committee has participated in a conference with representatives of the Farm Bureau Federation and has been invited to confer with a larger group composed of representatives of several national farm organizations that probably will meet during the month of September

At the conference held in July with representatives of the American Farm Bureau Federation, the broad outline of the farm bureau plan to promote better rural health was fully discussed It seemed to be apparent that the Farm Bureau Federation, like other influential farm groups, is opposed to compulsory federal legislation and is seeking means of accomplishing on a voluntary basis improvement and assistance of medical service for the farm population It appeared to be the consensus that practical application of proposed plans should be on a state and county level.

The Committee on Rural Medical Service of the American Medical Association was informed that the American Farm Bureau Federation is sending a letter to its component state bureaus suggesting appointment of rural health committees to confer with similar committees representing constituent state medical associations The Committee on Rural Medical Service agreed to communicate with the secretaries of all constituent associations and express the hope that each state association would appoint a committee on rural medical service that would be available for conferences with committees of the American Farm Bureau Federation and all other farm organizations since all planning for rural health improvement must have the benefit of the experience and advice of the organized medical profession It is respectfully suggested that you bring this matter to the attention of the proper local body of your association at the earliest possible time

Please advise me as to any action that may be taken with respect to the appointment of a committee on rural medical service so that results may be correlated by this committee

Very sincerely yours

(Signed) F S CROCKETT M D Chairman
Committee on Rural Medical Service
American Medical Association

It was regularly moved and seconded that the Council authorize the President to appoint a committee for the purposes set forth in this letter It was so ordered by vote of the Council

At the direction of the President the Secretary read the following letter

September 24, 1945

Dr Reginald Fitz
319 Longwood Avenue
Boston Massachusetts
Dear Dr Fitz

Mr Cahalan has asked me to write to you stating that the Blue Cross will be very happy to work with the Massachusetts Medical Society to enable the members of the Society to form a Blue Cross group We feel that it will be perfectly possible and very desirable to make arrangements whereby doctors who are not enrolled will have the opportunity to become Blue Cross members Physicians who might wish to transfer from certain groups through which they now hold membership to the Massachusetts Medical Society group would be allowed to do so

Of course it should be understood that a satisfactory method of payment would have to be evolved and perhaps the best way would be to have the Society bill all those who become Blue Cross members for their Blue Cross dues at the same time they are billed for their Society dues

Perhaps the members of the Society would like to protect themselves and their families against surgical and obstetric bills through membership in the Blue Shield If so we could work out an arrangement similar to the one we suggest for the Blue Cross We are aware of the courtesy privileges extended to the members of the profession but we have had some instances where doctors have asked to be covered by Blue Shield if membership in the plan was possible

Sincerely yours

(Signed) E. J. CUNNINGHAM
Director of Enrollment
Massachusetts Hospital Service

Under the Council rules the President referred this communication to the Committee on Public Relations

At the direction of the President the Secretary read the following communication

October 1, 1945

Reginald Fitz, M D
319 Longwood Avenue
Boston Mass
Dear Dr Fitz

We wish to employ at the Newton Hospital a doctor who has only a dental degree For a number of years he was engaged in the practice of oral surgery in Boston retiring before the war Since Pearl Harbor he has put in a little over a year as a volunteer anesthetist has carried out that work very efficiently and has met the approval of the surgeons with whom he has worked

Our question is Is it proper for a man possessing a dental degree to work as an anesthetist in the Newton Hospital under my supervision? We would appreciate an early answer Thanking you I am

Sincerely yours

(Signed) R S HUNT M D
Anesthetist-in-Chief

Under the rules, the President referred the communication to the Committee on Ethics and Discipline

At the direction of the President the Secretary read the following letter

September 21 1945

Dr R Fitz, President
Massachusetts Medical Society
8 The Fenway
Boston Massachusetts
Dear Dr Fitz

The American Epilepsy League has for some years been instrumental in making it easier for people suffering with convulsive disorders to get in touch with a qualified physician for their treatment With the great number of servicemen returning with a diagnosis of epilepsy the Veterans Administration has turned to us for advice in suggesting men capable of handling epileptics in the rural districts of Massachusetts At the present time, our referral list for Massachusetts is limited only to specialists

I am sure that you can understand the importance of this request and our sincere desire to fulfill it We are turning to you as president of the Massachusetts Medical Society for advice in the best manner for compiling such a list

As you undoubtedly know it is not necessary that a physician be a specialist in neurology to help epileptic sufferers There are many instances where the up-to-date knowledge of treatment is not known The League is in a position to put interested doctors in touch with these developments

If a personal interview with you or telephone conversation will clarify my request in any way I shall be delighted to see you Because of the urgency of this matter may I ask that you give it your attention at the first possible moment

Sincerely yours,

(Signed) ESTHER C. WALTHER, Executive Secretary
American Epilepsy League, Incorporated

Under the rules, the President referred this letter to the Committee on Public Health

Dr Basil E Barton, Norfolk, acting for the Norfolk District Medical Society, offered the following resolution

RESOLVED That the president of the Massachusetts Medical Society be requested to refer to the appropriate committee a request to investigate the fee schedule of the Massachusetts Industrial Accident Board with a view to raising fees for such as indicated

This resolution was referred by the President, under the rules, to the Committee on Public Relations

Dr Charles E Mongan, Middlesex South, offered the following resolution

WHEREAS The question has been repeatedly asked in public and private concerning the facilities of medical education in New England, and

WHEREAS, No satisfactory scientific answer has been forthcoming, therefore be it

RESOLVED, That the Massachusetts Medical Society undertake a survey of the medical educational facilities at present available in New England

mittee, as well as that of the OPA Regional Office, so ably managed by Miss Elizabeth Golden, the food rationing specialist of that office

Rations for service men on convalescent furloughs are now issued by five military rationing boards in New England, and the medical problems of members of the armed forces will from now on be handled by service doctors

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This committee has always issued extra rations according to its own views, guided by the best advice available, regardless of whether cases fell outside of the narrow list of diseases prescribed by the National Research Council, and it is a source of satisfaction that the latter has recently given an opinion that medical committees should function according to their own experience

This committee has always recognized the possible need of extra rations after hemorrhage or with anemia of any type below certain hemoglobin and red-blood-count levels, with various types of allergy, and, indeed, wherever a need could be shown to exist regardless of diagnosis. Thus, the need for extra protein in the later months of pregnancy has been demonstrated, as has also the efficacy of the Schemm diet in certain forms of heart disease

Local advisory committees are now functioning in Brookline, and, through the good offices of Dr. Guy Richardson, chairman of the War Participation Committee, in Brockton, Scituate, Lawrence, Pittsfield, Springfield, New Bedford, Worcester, Holyoke, Quincy and Lowell

The work of the Regional Office continues, nevertheless, to increase. Thus, in April, 1305 cases were processed, in May, 1322, in June, 1499. Something under half of these applications seem to merit approval. Cases from outside Massachusetts increased from 17 in May to 131 in June, mostly from Vermont, which seems to prefer the advice of the Massachusetts committee to the appointment of a committee of its own

The ending of the war has produced marked changes in the food rationing program — processed foods are no longer rationed, the rationing of meats and fats has been relaxed, and there is promise of an early ending of all food rationing except that of sugar

Your committee hopes that its duties will cease within the next few weeks, in the meantime, meat, fat and sugar rationing render a continued oversight necessary

This report is offered for the information of the Council

The Secretary moved the adoption of the report. This motion was seconded by Dr. Chapin, and it was so ordered by vote of the Council

War Participation Committee — Dr. Guy L. Richardson, Essex North, chairman

Dr. Richardson submitted the following report

Since our last report, physicians' committees to assist the rationing boards in Holyoke and Quincy have been organized

The only other matter of importance was a request from the Division of Employment Security of Massachusetts to approve a certificate form for veterans' disability, and to assist them by reviewing any questionable certificate. The certificate form presented was approved, and the committee voted to review any such certificate referred to us. This is the same procedure followed in the case of doctors' certificates for change of job, handled by the War Manpower Commission

With the war over, this committee asks for its discharge.

Dr. Richardson moved the acceptance of the report. This motion was seconded by Dr. Collins, and it was so ordered by vote of the Council

Dr. Fitz said that this report contained one recommendation, namely, that the committee be discharged. It was moved and seconded that this

recommendation be adopted and that this motion include an expression of gratitude from the Society to the members of the committee for having contributed so valuably to the war effort. It was so ordered by vote of the Council

Military Postgraduate Committee — Dr. W. Richard Ohler, Norfolk, chairman

Dr. Ohler offered the following report

Since last February, programs have been conducted as usual. Seventy-nine meetings have been held at eighteen installations scattered through New England

Up until the present moment, no final decision has been made regarding the termination of these programs throughout the country. It is assumed, however, that programs will cease at an early date. In the meantime, your committee and also the larger committee representing all the New England states are prepared to carry on

By way of an addition to this report Dr. Ohler said that this work of postgraduate instruction will cease throughout the country in December and that it is the intention of his committee to carry on until that time

He moved the acceptance of the report. This motion was seconded by Dr. Root, and it was so ordered by vote of the Council

Committee on Maternal Welfare — Dr. Raymond S. Titus, Norfolk, chairman

In the absence of the chairman, the Secretary read the following report

On August 23 a meeting of the Committee on Maternal Welfare was held at the Boston Medical Library. The purpose of this meeting was organization. At this meeting a report on the EMIC program by a subcommittee of the Committee on Maternal Welfare was submitted

This subcommittee wrote to the secretaries of the various districts of the Society asking for their reaction to the EMIC program. A reply was obtained from only two district secretaries. One report was favorable, and the other district society expressed its unqualified disapproval. Dr. McKay, who was present at the meeting, said that more than 50 per cent of the physicians in the state had participated in this program and that the results of the obstetric care, as reflected in maternal mortality, were excellent. The EMIC program will run for another year and a half, and reports of its progress will be made to this committee. The committee voted that the chairman should get in touch with Dr. Ohler relative to the refresher program. No elaborate program was deemed possible because of the continued lack of manpower due to the large number of men still in the service

The Secretary moved the acceptance of the report. This motion was seconded by Dr. Chapin, and it was so ordered by vote of the Council

Other Special Committees

Dr. Leavitt moved that a report of "no report" be accepted from the following special committees: Cancer, Council Rules, Expert Testimony, To Meet with Massachusetts Hospital Association, Physical Medicine and To Recommend Blue Shield Directors. This motion was seconded by Dr. Phippen, and it was so ordered by vote of the Council

APPOINTMENT OF AUDITING COMMITTEE

The following Auditing Committee was nominated by the President: William B. Robbins, Suffolk, chair-

The President, under the rules, referred Dr. Welch's statement to the Committee on Postwar Planning.

The President announced that the Council had completed its business and that he would entertain a motion to adjourn. Dr. Phippen made such a motion. This motion was seconded by Dr. Leavitt, and it was so ordered by vote of the Council.

The President announced the Council adjourned at 1.50 p.m.

MICHAEL A. TIGHE, *Secretary*

APPENDIX NO. 1

ATTENDANCE OF COUNCILORS

BARNSTABLE

C. H. Keene
W. D. Kinney

BERKSHIRE

I. S. F. Dodd
C. F. Kernan
Solomon Schwager
Helen M. Scoville
P. J. Sullivan

BRISTOL NORTH

W. H. Allen
J. H. Brewster
R. M. Chambers
W. J. Morse
J. L. Murphy
W. M. Stobbs

BRISTOL SOUTH

G. W. Blood
R. B. Butler
J. E. Fell
Henry Wardle

ESSEX NORTH

E. S. Bagnall
R. V. Bakerel
E. H. Ganley
H. R. Kurth
P. J. Look
G. L. Richardson
F. W. Snow
C. F. Warren

ESSEX SOUTH

H. A. Boyle
D. S. Clark
Loring Grimes
B. B. Mansfield
O. S. Pettingill
W. G. Phippen
E. D. Reynolds
H. D. Stebbins
P. E. Tivnan
C. F. Twomey
C. A. Worthen

FRANKLIN

H. M. Kemp
J. E. Moran

HAMPDEN

F. H. Allen
E. P. Bagg
W. A. R. Chapin
E. C. Dubois
Fredenc Hagler

F. S. Hopkins

Charles Jurist
M. W. Pearson
A. G. Rice
A. H. Riordan
G. L. Schadt
J. A. Seaman

HAMPSHIRE

H. A. Tadgell

MIDDLESEX EAST

J. L. Anderson
Richard Dutton
E. M. Halligan
D. L. Joyce
R. W. Layton
M. J. Quinn
W. F. Regan
R. R. Stratton

MIDDLESEX NORTH

J. J. Cassidy
H. R. Coburn
W. M. Collins
D. J. Ellison
A. R. Gardner
W. F. Ryan
M. A. Tighe

MIDDLESEX SOUTH

E. W. Barron
J. M. Baty
J. D. Bennett
W. O. Blanchard
G. F. H. Bowers
Alice M. Broadhurst
Madelaine R. Brown
R. N. Brown
R. W. Buck
E. J. Butler
H. F. Day
C. L. Derick
J. G. Downing
C. W. Finnerty
H. Q. Gallupe
F. W. Gay
H. G. Giddings
J. L. Golden
Eliot Hubbard, Jr.
F. R. Jouett
E. E. Kattwinkel
A. A. Levi
A. N. Makechnie
Dudley Merrill
C. E. Mongan
G. M. Morrison
J. P. Nelligan
E. J. O'Brien, Jr.
Dwight O'Hara

S. H. Remick
Max Ritvo
E. H. Robbins
M. J. Schlesinger
E. W. Small
A. B. Toppin
J. E. Vance
B. S. Wood
Hovhannes Zovickian

NORFOLK

B. E. Barton
Carl Bearse
Arthur Berk
M. I. Berman
J. H. Cauley
G. L. Doherty
Albert Ehrenfried
H. M. Emmons
Susannah Friedman
B. A. Godvin
J. B. Hall
H. B. Harris
R. J. Heffernan
P. J. Jalmauh
I. R. Jankelson
C. I. Kickham
H. M. Landesman
D. S. Luce
F. P. McCarthy
H. L. McCarthy
R. T. Monroe
F. J. Moran
Hyman Morrison
D. J. Mullane
J. J. O'Connell
W. R. Ohler
G. W. Papen
S. A. Robins
D. D. Scannell
L. A. Sieracki
Kathlyne S. Snow
S. L. Skvirsky
I. W. Spellman
J. P. Treanor, Jr.
N. A. Welch

NORFOLK SOUTH

C. S. Adams
D. L. Belding
Harry Braverman
F. W. Crawford
Frederick Hinchcliffe
E. K. Jenkins
N. R. Pillsbury
D. B. Reardon

PLYMOUTH

P. H. Leavitt
C. D. McCann
G. A. Moore
B. H. Pearce
W. H. Pulsifer

SUFFOLK

A. W. Allen
W. H. Blanchard
W. J. Brickler
W. E. Browne
A. M. Butler
David Cheever
N. W. Faxon
Reginald Fitz
Somers Fraser
Maurice Fremont-Smith
Channing Frothingham
F. C. Hall
A. A. Hornor
H. A. Kelly
R. I. Lee
C. C. Lund
W. J. Mixer
Donald Munro
H. F. Newton
R. N. Nye
F. R. Ober
F. W. O'Brien
J. P. O'Hare
L. E. Parkins
L. E. Phaneuf
Helen S. Pittman
J. H. Pratt
W. H. Robey
H. F. Root
R. M. Smith
E. F. Timmins
J. J. Todd
S. N. Vose
Conrad Wesselhoeft
C. F. Wilinsky

WORCESTER

C. R. Abbott
B. H. Alton
A. W. Atwood
F. P. Bousquet
W. P. Bowers
E. J. Crane
J. M. Fallon
L. M. Felton
J. V. Gallagher
L. P. Leland
W. F. Lynch
J. C. McCann
A. E. O'Connell
H. L. Paine
O. H. Stansfield
T. L. Story
J. C. Sullivan
R. J. Ward
B. C. Wheeler

WORCESTER NORTH

H. C. Arey
D. B. Cheatham
C. B. Gar
G. P. Keaveny
J. V. McHugh

APPENDIX NO. 2

REPORT OF THE EXECUTIVE COMMITTEE OF THE COUNCIL

The Executive Committee of the Council has held three meetings since its last report of January 31, 1945.

A meeting held on May 25 was in lieu of the annual meeting of the Council. The wartime restrictions imposed by the Office of Defense Transportation made the Council meeting impossible. The transactions of this meeting are set forth in the July 26, 1945, issue of the *New England Journal of Medicine*.

By way of explaining the purpose of this resolution, Dr Mongan said that the question concerning the facilities for medical education in New England frequently arose in the sessions of certain of the committees of the Massachusetts Legislature and that no satisfactory answer had been forthcoming. It had been said, he continued, that New England could stand one more first-class medical school. He added that the only way in which the truth of this statement could be determined would be through a survey as provided for in the resolution.

Under the rules, the President referred this resolution to the Committee on Medical Education.

Dr Harold R. Kurth, Essex North, offered the following resolution:

That the Massachusetts Medical Society recommend to the State Board of Registration in Medicine that it initiate such procedures as lie within its jurisdiction to eliminate chiropractic practice in the Commonwealth of Massachusetts.

In support of this resolution Dr Kurth said that all are aware that there is scarcely a town or city in Massachusetts in which there is not at least one or two practicing the chiropractic form of medicine. Dr Kurth added that he was offering this resolution in the name of the Essex North District Medical Society. Under the rules, the President referred the resolution to the Committee on Legislation.

Dr Phippen suggested to the Committee on Council Rules that provision be made whereby the report of the Executive Committee to the Council contain a résumé of the discussions which took place in the committee on particularly important matters. He pointed out that, if this were done, much time and discussion might be saved in the meetings of the Council. The President referred this suggestion to the Committee on Council Rules.

Dr Norman A. Welch reported for the Blue Shield as follows:

This is simply a report of information for you on behalf of the Blue Shield. I am making part of the report for Doctor McCann in order that there will be no delay by having two people speak on the subject.

The Blue Shield is progressing very satisfactorily, both financially and from the standpoint of increased subscriber membership. As of September 25, 1945, there were 183,190 participants consisting of 81,000 contracts. On December 31, 1943, there were 30,000 subscribers. This number jumped to 70,000 by December 31, 1944, and so far this year 113,000 members have been enrolled. From these figures, you can see that the enrollment in nine months of 1945 has exceeded the combined enrollment of both 1943 and 1944.

The important thing which I want to bring to you on behalf of the president and directors of the Blue Shield is the prospective increase in benefits to subscribers. The original \$25,000 which was given by the Massachusetts Medical Society to start this program has not been touched. At the time that the plan was started, the Commissioner of Insurance required that the Blue Shield put aside 25 per cent of the premiums received until there was a reserve of \$225,000. The latest audited financial report available is that of July 31, 1945, at which time there was a reserve of \$219,016. I have been assured by Mr. Cunningham that the reserve is now well above the \$225,000 required

by the insurance commissioner, so that it appears it will now be possible to use, for other purposes, the 25 per cent of the premiums, which we have not been able to touch.

The expenses of operating the Blue Shield run in the neighborhood of 75 per cent of the premiums, and it is believed that the cost of adding medical care in the hospital will be below the remaining 25 per cent. Thus, it is felt that medical benefits may be added without increasing the cost of membership to the subscribers. We have a committee of physicians from various parts of the state that has taken up the question of adding medical benefits in the hospital to the Blue Shield program.

I have visited the headquarters of the plan in New Jersey and have talked with the medical director. He believes that we can add the medical benefits and remain well within the 25 per cent available for this purpose. At the present time, a rough contract for the addition of such benefits has been submitted to the insurance commissioner for approval. Any change in the contract, such as that contemplated, must be approved by him in order that the subscriber may be adequately protected against failure of the plan or against loss of service that he is supposed to get. The projected arrangement provides for the payment to physicians for medical care in the hospital beginning with the first day of hospitalization and extending for a period of two weeks.

In New Jersey the period of payment is three weeks, but under their plan they exclude payment for hospitalization of three days or less. The Blue Shield committee believes that the exclusion of the three days hospitalization is not advisable because of the necessity of this short period of time for diagnostic study in some cases. The feeling was that it would not be rendering satisfactory medical care to exclude a three-day diagnostic study period. In New Jersey they have found that 85 per cent of the patients with medical cases are hospitalized for three weeks or less. It is hoped, of course, that we may eventually extend the period of payment beyond two weeks, but it is considered wiser to maintain a sound financial setup when these benefits are first added.

The fees planned for the physician are a payment of \$5.00 for the first day and \$3.00 for each subsequent day up to the limit of two weeks. The restriction to payment covering two weeks' hospitalization protects the plan financially against cases with chronic diseases of the heart and blood vessels. A substantial number of such cases could impose a severe financial burden on the plan and also serve to make it more difficult to discharge these patients from the hospital if their doctor's fee is being paid.

In the matter of complications arising in the course of surgery and obstetrics, the medical payment is made for a period of two weeks from the time of expiration of the period of surgical or obstetric hospitalization. In other words, if the surgical contract covers hospitalization of sixteen or eighteen days, and a medical complication requires a hospital stay beyond that time, the payment to the medical man is taken care of for an additional time up to the limit of fourteen days.

There are some questions that have not yet been adequately answered in the proposed extension of benefits. One of these is the matter of the payment for contagious disease. In some sections of the Commonwealth these cases are hospitalized under the care of a salaried physician, but in other sections the private practitioner takes care of such cases on an isolation ward in a general hospital. In the latter instance it would seem that the physician should be paid for the care of contagious cases, whereas in the former instance, such a fee would represent double payment to the physician.

At the present time, it is not thought wise to include payment for consultation service. It may be that this will eventually be included in the coverage given to the subscriber, but we must be extremely careful that we do not affect the financial solvency of this plan in its early days by the addition of further benefits.

I believe that this covers the essential points involved in the extension of medical coverage to the subscriber under the Blue Shield program. It is hoped that, with the permission of the insurance commissioner, these benefits can be added to the contract within a comparatively short period of time, and that these will be added without any additional expense to the subscriber.

The second meeting of the committee was held on August 22. This was of an emergency character. It was held for the purpose of giving consideration to two items of business that were of pressing importance.

The first had to do with a fee schedule submitted by the Committee on Rehabilitation. This fee schedule (Appendix No. 3), after modification by the committee, was approved by the Executive Committee, as an emergency measure, in the name of the Council. Dr. Richard Dutton, Middlesex East, at his request, was recorded as disapproving.

The second item of business had to do with a request that came from the Society's delegates to the Council of the State Medical Societies of New England that the sum of \$100 be contributed toward defraying the expenses of this council. The committee, subject to review by the Committee on Finance, approved this appropriation in the name of the Council of the Massachusetts Medical Society.

The third meeting—the pre-Council meeting of the Executive Committee—was held on September 26, 1945.

The committee reviewed the reports that are to be considered by the Council. It recommends the acceptance of those that are purely informational. It recommends that those that contain recommendations be accepted and that the recommendations contained in them be adopted with one exception, namely, that in the case of the report of the Committee Appointed to Study a Possible Revision of the By-laws as They Relate to the Election of Fellows, it recommends that the words "if possible" appearing in the second recommendation be deleted and that the word "may" be inserted in the same recommendation between the word "committee" and the word "be."

The committee noted that certain recommendations, which appeared in the report of the Subcommittee on Public Information of the Committee on Postwar Planning, were withdrawn and that likewise withdrawn were the first and second recommendations, which appear in the supplementary report of the Committee on Postwar Planning.

The committee reviewed a joint report and resolution to be submitted to the Council by the Committee on Public Relations, the Committee on Legislation and the Committee on Postwar Planning.

The Executive Committee recognized that these withdrawals and the joint report and resolution represented an attempt to meet in the person of one individual the needs of the Society as expressed by these three committees. The Executive Committee unanimously recommends that the Council accept this latter report and adopt the resolution contained in it.

The committee has approved of the President's act in appointing two fellows of the Society to attend, at the Society's expense, a conference on public relations to be held in Chicago under the auspices of the Council on Medical Service and Public Relations of the American Medical Association.

The committee recommends that the War Participation Committee be discharged by the Council, with an expression of gratitude to its chairman and members for their valuable contributions to the war effort.

The Committee reviewed and approved the following ad interim appointments made by the President:

To the Committee on Industrial Health

Dr. Thomas L. Shipman, Essex South, chairman (a member of this committee from 1942)

To the Committee on Postwar Planning

Dr. Elmer S. Bagnall, Essex North

To the Subcommittee on Hospitals of the Committee on Postwar Planning

Dr. Harold Jeghers, Norfolk

To the Medical Advisory Committee to Regional OPA

Dr. F. Gorham Brigham, Norfolk

Representatives from the Society to the New England Medical Council

Dr. Dwight O'Hara, Middlesex South

Dr. Allen G. Rice, Hampden

Dr. Michael A. Tighe, Middlesex North

Representatives from the Society to the Massachusetts Central Health Council

Dr. James W. Bunce, Berkshire

Dr. Merrill E. Champion, Suffolk

Dr. George D. Henderson, Hampden

Dr. William D. Kinney, Barnstable

Dr. Robert B. Osgood, Suffolk

Dr. Roy J. Ward, Worcester

Representative from the Society to the Organization Known as "Mental Health for Victory"

Dr. Abraham Myerson, Norfolk

Representative from the Society to the Hospital Council of Boston for the Year 1945

Dr. William E. Browne, Suffolk

Representative from the Society to the Legislative Committee of the Massachusetts Central Health Council

Dr. William E. Browne, Suffolk

Representative from the Society to the Massachusetts Committee for Nurses Procurement and Assignment Service

Dr. Dwight O'Hara, Middlesex South

Representative from the Society to the Massachusetts Nursing Council for War Service

Dr. David D. Scannell, Norfolk

Representative from the Society to a Professional Advisory Committee Organized by the Division of Vocational Rehabilitation of the State Department of Education for the Purpose of Establishing a Program of Physical Restoration

Dr. Joseph H. Shortell, Suffolk

The printed circular of advance information contains a letter from the Committee on Rural Medical Service of the American Medical Association. In accordance with the request contained in the letter the Executive Committee recommends that the Council direct the President to appoint a committee of three to confer with a committee of the Massachusetts Farm Bureau Federation concerning rural medical service.

MICHAEL A. TIGHE, Secretary

APPENDIX NO. 3

FEE SCHEDULE SUBMITTED BY THE COMMITTEE ON REHABILITATION

This schedule was approved by the Executive Committee of the Council in the name of the Massachusetts Medical Society.

This approval was given in a special session of the Executive Committee held on August 22, 1945. The necessity for this action was based on the committee's judgment that an emergency was involved.

This schedule was offered to the Division of Vocational Rehabilitation of the Massachusetts Department of Education at the request of the division itself. This division will pay the medical-care costs of those individuals who have static and remediable physical difficulties and who, through their own efforts, cannot meet such costs. The individual receiving aid in this program need not show indigence.

I. EXAMINATIONS

A. General medical examination (see *Manual of Policies*, Chapter VIII) to include medical history and physical examination \$5.00

B. Examination by specialist 10.00

C. X-ray examination 5.00

Extremities 10.00

Hip, femur, shoulder 10.00

Skull 10.00

Spine (one section, as lumbar spine) 15.00

Spine (two or more sections, as lumbar and sacral) 20.00

Spine (entire, with cervical) 20.00

Barium meal—gastrointestinal tract 15.00

Barium enema 5.00

Urological—simple KUB 20.00

Urological—pyelography intravenous (with injection of medium) 25.00

Urological—pyelography retrograde 10.00

Chest 15.00

Gall bladder 15.00

D. Laboratory Examination.

Bacteriological 5.00

Cultural examination for fungi 2.00

Routine culture 5.00

Pus or exudate, cultural examination including classification of organism 5.00

Throat culture including classification of organism 5.00

Blood culture 5.00

Examination of smears 2.00

Pathological 5.00

Tissue examination 10.00

Frozen section, rush diagnosis at laboratory 5.00

Guinea pig inoculation 5.00

work (and we have no grievance with that) by the osteopaths, the Approving Authority was increased in membership to five, retaining the present members, consisting of the Commissioner of Education, the Commissioner of Public Health and the secretary of the Board of Registration in Medicine.

We would feel we had not done our duty did we fail to mention the amount of time devoted intelligently at the State House by Dr H Quimby Gallupe, representing the Board of Registration in Medicine. Dr Vlado Getting, the Commissioner of Public Health, was always well prepared to discharge his duties before various committees and did so in an efficient manner. It should here be stated that the officers of the Society and former officers lay persons, certain members of the House and Senate really worked hard in order that the House and Senate might have before these bodies information which should have been helpful in casting their votes. The work done by several of the district societies was outstanding. In all probability all the district societies did some work, although it was difficult to measure the effectiveness of the work which may have been done by two or three of the district societies. One of our mistakes may have been that we failed to use proper means to make articulate a great many of the members of the Massachusetts Medical Society. Probably many of these would have helped a great deal had we succeeded in reaching them. All members of the Society, however, through their district legislative committees, should have been acquainted with activities at the State House affecting in one way or another public health. A great many members did excellent work in personally interviewing members of the House and Senate. The family doctor was a vital force in proper personal interviews with members of the House in the matter of bills which would, had they passed, have aided substandard schools of medicine. On these bills alone we spent nine full days at the State House, not to speak of parts of days which were devoted to these bills. The vote, as you know, in the House was 148 to 74.

The day has gone by in which it was felt only a few needed to work, the present is here, and the work of those who have been active is insufficient, and the future is ahead. It will require concerted, articulate, letter writing membership to assert itself properly.

Some expenditure of money will be necessary and the amount should be determined by the Council. Really considerable sums as we consider money may have been spent by some groups. We are informed the osteopaths were asked to contribute considerable in order that their expenses might be paid, including the amount well earned by former Lieutenant-Governor Cahill. We paid no one in connection with osteopathy or chiropractic or any other bill more than a nominal sum which by no means paid for in full the work which was done by our legislative counsel, Mr Charles Dunn. We should not be called on to raise and spend money of our own when we are not asking for or seeking anything for ourselves personally, and when our sole aim so far as we are concerned is not only to preserve the present standards of the practice of medicine in this state but to raise those standards.

The Governor of the Commonwealth, after real study and after giving the matter the time it deserved, vetoed the Chiropractic Bill, and this veto says so much in regard to licensure generally we herewith insert it in our report.

The Commonwealth of Massachusetts
Executive Department, State House
Boston, July 20, 1945

To the Honorable Senate and House of Representatives

I am returning herewith without my approval House 1738 entitled "AN ACT ESTABLISHING THE BOARD OF REGISTRATION OF CHIROPRACTORS AND DEFINING ITS POWERS AND DUTIES."

The enactment proposes the establishment of an entirely new Board for the examination and registration of applicants seeking to practice a method of healing the sick. It would set up a new and different administrative method of regulating a branch of the practice of medicine as that term generally relates to the prevention, cure and alleviation of disease, the repair of injury or treatment of abnormal or unusual states of the human body and their restoration to a healthful condition. It would establish new and different standards of education and qualification for applicants seeking to practice in a field in which minimum standards are already established by statute. Thus, it would introduce into the statutory system a 'double standard' for the selection of practitioners in the field of medicine.

The object of regulatory legislation in the field of medical science heretofore adopted by the General Court is the promotion of the public good and the protection of our citizens against the evils normally resulting from the attempts of untrained and unskilled persons to practice the healing arts. The Legislature wisely has not granted exclusive

rights of practice to any particular method of healing. In Section 7 of Chapter 112 of the General Laws it is expressly declared that the statutory provisions relating to the examination and registration of applicants seeking to practice medicine 'shall not be held to discriminate against any particular school or system of medicine.' But just as wisely the General Court heretofore has recognized that as the knowledge of the science of medicine increases and methods of treatment of the ill improve the public good requires the new practitioner to be better informed and better equipped and accordingly, it has required that minimum standards of education and qualification be met by all applicants irrespective of the particular system or method of treatment they espouse. The beneficial effect upon our citizens generally of such a policy is clearly apparent. On a subject of so much importance to every one of the citizens of the Commonwealth, the legislative policy which has been so long pursued should not be halted or turned aside unless the public good clearly requires another course.

Such a policy has not prevented the development or practice of particular methods or systems of medicine nor has it denied to the public access to treatments prescribed by such systems. The osteopathic method, for example, has been and is now practiced in the Commonwealth under the provisions of the statutes relating to the practice of medicine. Similarly within the scope of the same legislative policy the chiropractic method should be practiced.

Respectfully,

(Signed)

MAURICE J TOBIN
Governor of the Commonwealth

Following passage of this bill, we held meetings and as a result of these Doctors Mongan, Spellman, Heffernan, Good, Doyle, Tighe, Wilinsky and Browne visited the Governor. It was his thought that the doctors of the Massachusetts Medical Society and others had not sufficiently set forth their views to the members of the House and the Senate. His Excellency did not tell us what he would do except to give the matter further study. He sent an attorney-at-law to meet with us and we honestly gave him our thoughts on this measure. We explained to the Governor that we felt we had in a proper way made our position on this matter as clear to the members of the Legislature as we had in the matter of bills affecting substandard schools. We know we were in communication with 179 of the 240 members of the House, and 38 of the 40 members of the Senate. We do not know what the chiropractors did that we did not do.

On the whole, the results of the year's work have been satisfactory. At the meeting held August 15 the committee voted that we recommend to the Council that a column in the *Journal* be devoted to these matters of legislation so that all the members of the Society may be abreast of the times. It was suggested that the chairman of the Committee on Legislation might edit this column. However, the Council may decide that. The Secretary of the Society has informed us that space in the *Journal* is ready for this now and has heretofore been available. The committee recommends a combined meeting of at least the executive groups with the Subcommittee on Public Information of the Committee on Public Relations and the Committee on Legislation in order that insofar as the practice of medicine is concerned the people of our state may know our thoughts and have our viewpoints. The Wagner-Murray-Dingell Bill lies ahead. The present chairman of the Committee on Legislation will later briefly discuss this Bill.

The retiring chairman is extremely grateful to his co-workers on the Committee on Legislation and to all others, and in a particular way the family doctor, for the help given.

W E BROWNE, Chairman

APPENDIX NO 5

REPORT OF THE COMMITTEE ON POSTWAR PLANNING

Meetings of the Committee on Postwar Planning, its Executive Committee and its subcommittees, have been held since the last meeting of the Executive Committee of the Council, and various subjects have been considered.

The need for a physician as secretary and educational director of the Society has been discussed. The duties of such a position might include, first, the development of services for returning medical veterans in relation not merely to their postgraduate training but to aiding them in other ways, such as providing information in regard to location for practice, and secondly be concerned not alone with postgraduate education within the membership of the Society but particularly with the Society's program for extending medical information to the public.

Representatives of the trustees, superintendents and chiefs-of-staff of ninety-eight hospitals in Massachusetts

Scaleniectomy	50 00
Nerve suture	100 00
Sympathectomy — cervical	175 00
Sympathectomy — thoracolumbar (unilateral)	150 00
Resection presacral plexus, resection of	100 00
Cistern puncture	50 00
Skull, decompression of	100 00
Tumor of brain	200 00
Gasserian ganglion, section of posterior root	150 00
Neuroma, excision of arm or leg	75 00
Neuroma, excision of finger or toe (single)	25 00
Neuroma, excision of finger or toe (multiple)	50 00
Operations — Orthopedic	
Amputations	
Shoulder	100 00
Upper arm	75 00
Forearm	75 00
Hand	50 00
Finger (one)	25 00
Each additional one	10 00
Hip	125 00
Thigh	100 00
Knee	100 00
Lower leg	75 00
Toe (one)	25 00
Each additional one	10 00
Arthroplasty	
Any major joint	150 00
Arthrodesis	
Any major joint	150 00
Joint resection	
Shoulder	150 00
Elbow	100 00
Wrist	100 00
Hip	150 00
Knee	100 00
Ankle	100 00
Joint dislocation — recurring (any major joint)	150 00
Other operations	
Spine fusion	150 00
Bone graft (for non union)	150 00
Bone drilling (for non-union)	75 00
Foot stabilization	150 00
Tendon repair (old case)	75 00
Supraspinatus tendon, repair of	150 00
Arthrotomy (any major joint)	100 00
Removal of bone plate	35 00
Hallux valgus (unilateral)	75 00
Hallux valgus (bilateral)	100 00
Hammer toe (one)	25 00
Sequester, removal of (superficial)	25 00
Sequester, removal of (deep)	125 00
Torticollis, operation for	100 00
Plaster Casts (not including first application with operation)	
Forearm	7 50
Whole arm	10 00
Shoulder spica	20 00
Leg to knee	7 50
Leg to groin	10 00
Hip spica	25 00
Plaster jacket	25 00
Plaster jacket (including head)	30 00
Operations — Miscellaneous	
Blood transfusion (not including cost of blood)	10 00
Adenectomy — cervical or inguinal (simple)	20 00
Adenectomy — cervical or inguinal (radical)	75 00
Adenectomy — radical (complete neck or groin)	150 00
Biopsy — lymph node, bone, skin or muscle	25 00
Biopsy — superficial structures	10 00
Biopsy — deep structures (node, bone breast or muscle)	20 00
Breast, resection of (simple)	75 00
Breast, resection of (radical)	150 00
Carcinoma of lower lip excision of (simple)	50 00
Carcinoma of lower lip, with neck dissection	150 00
Carcinoma of tongue, excision of	100 00
Dupuytren's contracture (radical)	100 00
Femoral artery, ligation of (unilateral)	50 00
Femoral vein, ligation of (bilateral)	75 00
Ingrown toenail excision of	20 00
Lumbar puncture	10 00
Pilonidal sinus, excision of	50 00
Tenotomy	25 00
Thyroid artery ligation of	75 00
Vena cava ligation of	150 00
Thyroidectomy — subtotal (bilateral)	125 00
Thyroidectomy — two-stage subtotal	150 00
Varicose veins — ligation of saphenous vein high	50 00
Unilateral	75 00
Bilateral	100 00
Varicose veins with ligation of perforating veins	100 00
Varicose veins, injection treatment of (each)	5 00
Varicose ulcer — excision and graft	100 00
Plastic operations — minor	75 00
Plastic operations — extensive	150 00

the operative fee is more than \$100 except in those cases wherein the assistant is a full-time employee of the hospital in which the operation is performed

III MEDICAL CARE

Medical care shall be placed at the disposal of such cases as are static and which, with adequate care, offer good prognoses

The fees for medical services in such cases needing hospital care and requiring the services of a physician devoting his time to a particular specialty, shall be at the rate of \$5 per day for the first week and \$25 per week for all subsequent weeks, provided the total charge does not exceed \$150

The fees for medical services in such cases treated by a general practitioner shall be at the rate of \$5 for the first visit, whether in the home, hospital or office, \$3 for each subsequent visit in the hospital or home, and \$2 for each subsequent visit to the physician's office, provided the total amount charged shall not be in excess of \$150

APPENDIX No 4

REPORT OF THE COMMITTEE ON LEGISLATION

The first meeting of this committee for the legislative year 1945 was held on December 26 and the last on August 15, on which date, following the resignation of W E Browne, of Suffolk, Humphrey L McCarthy, of Norfolk, was elected chairman for the year 1946. Between those two dates we considered and acted on nineteen bills in the Senate and fifty-one bills filed in the House. We reported to the Council on January 31 and to the Executive Committee, acting for the Council, on May 23, and from each of these bodies received approval without reservation for work done. A great majority of the members of the Society who read the pages of the *New England Journal of Medicine* are somewhat familiar with these bills affecting public health and action taken on these bills.

In the August 23 issue of the *Journal*, a comprehensive résumé may be found of the work done. Some members of the committee, and the chairman, had had no experience at the State House before January 1 of this year. We have had considerable experience since that time. The two reports of the committee referred to above, which have been printed in the *Journal*, make repetition of our activities unnecessary. We unfortunately made mistakes and we have some recommendations. With information available to us at the first of the year, and with insufficient time to get more, we were unable to discuss clearly at times some matters with the Public Health Committee, the Committee on Education, and the Ways and Means Committees of the House and the Senate, and to give to these committees information which they asked. We did not know, for example, the status of chiropractors licensed in some degree and permitted to practice in forty-three states in the country, nor did we have a comprehensive knowledge of licensure affecting osteopaths. The chairman has sent a questionnaire to each licensing board and state medical society and from each, without exception, has received nearly complete answers as to their methods and degrees of grades of licensure of chiropractors, osteopaths and regular practitioners of medicine, and information received will certainly be helpful in the future.

It was noted that in matters of legislation affecting particularly certain groups, those representing such groups who were well prepared to discuss their measures at times fared better than the rest of us, for example, the Massachusetts Medico-Legal Society, under the direction of Dr Peirce H. Leavitt, which had enacted desirable laws affecting medical examiners, and those under the direction of Dr Sidney Farber, who finally, by a close shave, had maintained present laws in regard to vivisection, changes in which, as proposed, would ultimately have harmfully affected the health of our people in a serious manner.

It probably is correct to say that in the matter of osteopathy, the single measure obtained and which is now law may be considered by some to have lowered in some degree standards by which persons may practice medicine in this state. Perhaps in the near future the Legislature will be asked its judgment in grading the practice of osteopaths, which in many ways seems necessary. In some states, as you may know, osteopaths according to the training they may have are graded as to things they may do. Under the direction of former Lieutenant-Governor Cahill, who was paid for his

In the above cases when the fee is \$100 or less, two weeks' aftercare is included. In cases in which the fee is over \$100, three weeks' aftercare is included.

Extra visits when necessary beyond the stated periods shall be at the rate of \$3 for a house or hospital visit and \$2 for an office visit.

When an assistant is deemed necessary he shall be allowed a fee of \$10 in all cases wherever the operative charge is \$100 or less and 10 per cent of the operative fee in all cases wherever

(3) That the State Committee on Membership, acting within the by-laws, invite an officer of the district society or a member of the district committee on membership to review with them the record of an applicant before final decision of disapproval of such an applicant is made

It is the opinion of your committee that the above recommendations will result in elimination of any misunderstanding that has occurred in the past between the State Com-

mittee on Membership and the district committees on membership

CHARLES I. KICKHAM, *Chairman*
WILLIAM A. R. CHAPIN
C. BERTRAM GAY
PEIRCE H. LEAVITT
DONALD MUNRO
DANIEL B. REARDON
MICHAEL A. TIGHE

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D. *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 31511

PRESENTATION OF CASE

A forty-six-year-old crane operator was admitted to the Emergency Ward in a semi-stuporous condition. The history was obtained from his wife.

Four days before admission, while eating breakfast the patient was suddenly seized by a severe shaking chill and his temperature rose to 102°F. A physician prescribed a sulfonamide, milk of magnesia and paregoric. He had several more shaking chills that day. At the same time vomiting and severe diarrhea developed. Until the time of admission he continued periodically to vomit yellow, thin fluid and had eight to ten copious bowel movements a day. The stools were watery and cloudy. He developed an intense craving for water. During the period of his illness he had passed no urine. He had not complained of pain. About twelve hours before admission he had a large watery stool and soon after collapsed remaining unconscious for a short time. The systolic blood pressure at that time was said to have been about 40.

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it has been as high as 50 or 60 per cent. I am sure that the mortality is largely influenced by the fact that many of these patients suffer from other debilitating diseases or from chronic malnutrition, such as the cases found in the German prison camps, the dysentery being merely the terminal event. It seems to me remarkable for an otherwise healthy man in a community where bacillary dysentery is not endemic to have been stricken by such an acutely fatal type of the disease. Furthermore, patients with even mild bacillary dysentery have a good deal of abdominal pain as well as bloody stools, neither of which this patient had. I do not know how accurately the stools were observed, nor do I know that any were examined here in the hospital, but it would be unusual for a patient dying of bacillary dysentery not to have some pain and usually a good deal of blood in the stools. For that matter, any acute intestinal infection leading to such a rapidly fatal termination would be expected to have abdominal pain to a considerable degree, as well as bloody stools. I am forced to overlook the absence of these two findings in this patient, the history perhaps being unreliable and the stools not accurately observed.

The same objections can be applied to a disease somewhat more frequently found in this community, namely, amebic dysentery. Amebiasis, as we all know, is apt to run a much more chronic course than this, but there is an acute form that is rapidly fatal, although I have never heard of one dying quite so rapidly as this. I see no way of distinguishing between the two types, except on laboratory evidence, which is not available. I presume that the patient was in the hospital such a short time that no stool cultures were obtained. At any rate if they were, they probably were not reported until after death.

There is one other type of acute infection of the gastrointestinal tract that is much oftener found here, namely, acute ulcerative colitis of the idiopathic type. It can occasionally run an extremely fulminating course. I have never heard of a patient's dying within four days of the onset, although I can recall one who died within ten days. Those cases usually manifest signs of fulminating sepsis and have marked disturbance of the gastrointestinal tract, with abdominal pain and bloody stools. The absence of bloody stools, however, in the idiopathic type of ulcerative colitis is somewhat less disturbing than in the other two diseases that I have mentioned. I believe that this patient had some form of ulcerative colitis, some infection of the gastrointestinal tract. I do not see how one can distinguish on clinical grounds whether it was of the idiopathic variety or whether it was bacillary or amebic. In the absence of the laboratory investigation one can only guess concerning the etiology.

In a patient dying as rapidly as this from such an acute and severe diarrhea, I think that one has

a right to inquire whether poisoning played a role, particularly since the symptoms came on while eating breakfast. The two most frequent types of poison that would be expected to produce a picture like this are arsenic and mercury. I do not see any way to exclude them. In a patient coming in with this picture one has to keep poisoning in mind. So far as arsenic goes, which is somewhat likelier than mercury, if it were administered while he was having breakfast one would not expect the symptoms to come on so soon. Usually several hours elapse, whereas with mercury, the intestinal symptoms come on sooner. Either can produce this picture, with diarrhea, shock and hemoconcentration and renal suppression. Somewhat against poisoning as a possible cause is the fact that the patient's illness started with chills and fever, making it much likelier that an acute infectious process was behind it all.

While we are on the subject of poisoning, I think that it would be relevant to inquire what possible role the sulfonamides played in the production of the urinary suppression. We are told that this patient was anuric from the onset of his illness, which seems to indicate that sulfonamides probably played no role. Certainly the urinary picture could have been the logical result of the disease without the additional effect of the sulfonamides. If chemotherapy played any role, one would like to know several things not listed in the history. One would like to know what preparation was administered. If sulfaguanidine were used, one would not expect it to have a deleterious effect on the kidneys. On the other hand, sulfadiazine in a patient as dehydrated as this one was might produce considerable damage. One would also like to know whether he retained the sulfonamide. Since he was vomiting, it is conceivable that medication was not retained. In the absence of any additional information, all I can do is to mention the possibility of tubular damage secondary to sulfonamide administration, I see no way of settling the problem.

DR RONALD C. SNIFFEN: There was a trace of sulfadiazine in the blood.

DR KRANES: Apparently some of it was retained. It remains to consider whether any lesion outside the gastrointestinal tract could have been responsible for the chain of events described here. I cannot think of anything of this sort that explains the picture to my complete satisfaction. There is one thing that ought to be mentioned, namely, acute adrenal insufficiency. Patients with Addison's disease in whom an acute adrenal crisis develops have exactly this picture, — severe nausea, vomiting and diarrhea with enormous fluid loss, — go into shock with renal suppression and die in this manner. It would explain many of the things that the other diagnoses do not explain, particularly the absence of blood in the stools. But I do not see how we can make such a diagnosis in the absence

of any confirmatory finding. No mention is made of pigmentation, nor are we told anything about the previous state of health. It would be unlikely for acute adrenal insufficiency to manifest itself as suddenly as this. Furthermore, the onset with chills and fever is decidedly against it.

So far as any disease above the diaphragm is concerned, I do not see how anything in his heart could have been responsible. To be sure, we have mention of a to-and-fro pericardial friction rub. That may or may not have been present, and even if it were, it can be explained on the basis of the uremia, since many patients dying of uremia develop a sterile pericarditis. So far as a lesion in the lung goes, I cannot quite reconcile it with the rest of the picture. May we see the x-ray film of the chest?

DR. CLAYTON H. HALE: This film was taken under considerable difficulty and is not satisfactory. It was taken in expiration while the patient was sitting in bed. There is no definite disease demonstrated anywhere in the lung. The heart has been pushed up considerably by the high diaphragm.

DR. KRANES: Concerning the rales heard in the chest, it is not unusual for moribund patients such as this to show a certain amount of moisture in their lungs. It does not necessarily indicate an inflammatory exudate.

In conclusion, I can make no other diagnosis than some acute ulcerative infection of the gastrointestinal tract. On the basis of probability in this community, an idiopathic type of ulcerative colitis is the likeliest condition, bacillary dysentery is less likely.

DR. WILLIAM BECKMAN: I was asked to see this man late in the evening. No record had been written at that time, and my remarks were therefore not recorded. The thing that struck me most was his respiratory distress.

DR. KRANES: The rate was 20.

DR. BECKMAN: I did not count the respirations but I should have said that they were faster than that. I was probably wrong, but I thought that he had a massive pulmonary embolus. To know that he did present respiratory distress may influence your opinion.

DR. KRANES: I do not believe so. If this patient did have an acute infection in the lungs, such as pneumonia, it is difficult for me to reconcile such an infection with the gastrointestinal symptoms. One thing that did occur to me was the possibility of some acute surgical condition in the abdomen. Since you have mentioned an acute pulmonary embolus, the thought comes to mind that this man might have had an acute mesenteric thrombosis. If he did, it was a most unusual one.

DR. SNIFFEN: Dr. Berg, you also saw this man. Have you anything to add?

DR. ROBERT BERG: I thought that the whole picture was that of a man who had chills and fever

and other evidence of infection and then went into shock and died. We thought that he had an overwhelming infection. We considered cholera and asked his wife about the nature of the stools. When specifically asked, she said, "Yes, they were rice water in character." But it was a leading question and could not be relied on. We thought that he might have had dysentery, but that is as far as we could go.

DR. GEORGE COTZIAS: Dr. Charles A. Janeway, when seeing a similar patient in consultation, said that with a severe gastrointestinal upset but with no blood in the stools and no tenesmus or cramping one must think of scarlet fever, influenza and meningitis. These conditions are quite frequently missed in patients presenting this picture.

DR. DONALD S. KING: Could liver disease have caused the diarrhea?

DR. KRANES: I do not see how liver disease could logically have explained the symptoms.

DR. KING: Neither can I.

DR. MILTON H. CLIFFORD: Does not cholera respond quite rapidly to sulfonamides?

DR. KRANES: I do not know. I have never seen a case but I do not believe that we even need to consider cholera.

DR. RICHARD J. CLARK: Since there were scleral hemorrhages and possibly a pericarditis, what about an overwhelming pneumonia with a renal complication on top of that?

DR. KRANES: I attribute the scleral hemorrhages to persistent vomiting, but I may be wrong in doing so. I believe that any acute overwhelming infection, regardless of its nature, may produce nonspecific gastrointestinal symptoms, in other words, it is not necessary to postulate a primary lesion in the gastrointestinal tract to give this picture. Further than that, what sort of overwhelming infection he might have had is a pure guess.

CLINICAL DIAGNOSIS

Bacillary dysentery

DR. KRANES'S DIAGNOSIS

Acute ulcerative colitis, idiopathic type

ANATOMICAL DIAGNOSIS

Acute hemorrhagic interstitial pneumonia

PATHOLOGICAL DISCUSSION

DR. SNIFFEN: At autopsy, one was impressed by the signs of toxicity. The liver was enlarged and friable, the splenic pulp was mushy, and the various lymph nodes were hyperplastic. The gastrointestinal tract was normal except for a striking hyperplasia of the lymphoid tissue. The kidneys were swollen and soft. Petechial hemorrhages had occurred beneath the endocardium of the left ventricle. The pericardial cavity was normal. At first glance the lungs seemed to blend into the general background, for they were wet with a hemorrhagic fluid. Yet they were a little too firm and

airless to be merely hyperemic and edematous, and the right middle lobe was practically normal. Our suspicions were confirmed by the sections, which showed microscopically a severe hemorrhagic interstitial pneumonia. The bacteriologic studies were inconclusive, since the lungs had been sectioned before cultures were taken, colon bacilli and an anaerobic streptococcus grew out.

I have reviewed sections of lungs removed at autopsy in this hospital during the influenzal epidemic of 1918, and the sections from this case compare favorably with them and with the reports in the literature. The alveolar walls were hyperemic, and the interstitial exudate consisted predominantly of mononuclear cells, with pronounced edema and hemorrhage into the alveolar walls and spaces. In contrast to this there was a purulent bronchitis, with polymorphonuclear cells infiltrating the bronchial walls and sometimes the neighboring alveoli.

We do not pretend that this was a case of influenza pneumonia, but it was one of fulminating hemorrhagic pneumonia.

DR KRANES: Did you do a post-mortem blood culture?

DR SNIFFEN: Yes, it showed the same organism as the lungs, and we could draw no conclusions.

DR KING: Was the cyanosis the ashen gray type that we saw with influenza?

DR BECKMAN: It did not seem so to me.

DR KING: In the influenza epidemic one could almost diagnose the disease from the character of the cyanosis.

DR BECKMAN: He looked like a patient with massive pulmonary embolism who was in collapse.

DR W WILSON SCHIER: Did the adrenal glands show any damage?

DR SNIFFEN: No.

CASE 31512

PRESENTATION OF CASE

A fourteen-year-old schoolgirl was sent to the hospital because of marked difficulty in speaking.

Prior to the present trouble the patient had apparently been quite well. Approximately five months before entry she noticed that articulation was becoming progressively more difficult. At that time she also began to salivate excessively. Her physician prescribed pills, but these did not relieve her. Three weeks before entry visual perception of distant objects was reduced, but she was able to read quite well. On three successive mornings she had vomited, she had not felt nauseated, and the vomiting was not projectile. Two months before entry the patient began to feel dizzy while walking, she tended to reel, stagger and bump into objects but did not fall. Her parents noticed a "side-to-side movement" of the eyes. At that time she also complained of gagging and

coughing while drinking fluids. Only once, and then for just an hour in the morning, did she have a headache. There was no tinnitus, loss of hearing, diplopia, paresthesia or numbness of the face or extremities, nor any weakness of the extremities. She was able to maintain satisfactorily her scholastic progress in the second year of high school.

The family and past histories were noncontributory.

Physical examination disclosed a well developed but poorly nourished adolescent girl who seemed quite comfortable. Her voice had a thick nasal quality. Vision was 20/70 in both eyes, correctable to 20/50 with a pinhole. The fundi were normal. There was a vertical nystagmus, as well as a horizontal nystagmus, on left lateral gaze. The patient could read best with her head tilted to the right and backward, thereby reducing the nystagmus. The left pupil was 6 mm in diameter, and the right 5 mm. Both were round and reacted well to light and accommodation. There was no diplopia. Ocular movements were normal. There was slight weakness of the muscles on the left side of the face, and the patient could not whistle. Hearing was not impaired. Finger-to-nose and heel-to-shin tests brought out slight unsteadiness on the left side, they were normal on the right. There was no tremor of the extremities. The palate deviated to the right, and the gag reflex was absent. The patient choked on drinking water. The tongue could be extended only a few millimeters. There was weakness of flexion and rotation of the head and neck. There were no sensory disturbances or weakness of the muscles of the extremities. The abdominal reflexes were slightly reduced on both sides, and the plantar reflexes were equivocal. The arm, knee and ankle jerks were normal. The patient walked on a broad base with a reeling gait and had a tendency to stagger or fall to the left. The Romberg test was negative. The heart, lungs and abdomen were normal.

The temperature was 98°F, the pulse 92, and the respirations 20. The blood pressure was 110 systolic, 70 diastolic.

Examination of the blood revealed a hemoglobin of 14.0 gm, and a white-cell count of 6600, with 73 per cent neutrophils. A blood Hinton test was negative. The urine was normal. X-ray studies of the skull, cervical spine and chest were negative. A lumbar puncture demonstrated an initial pressure equivalent to 120 mm of water, which rose to 150 mm after compression of both jugular veins. This did not drop when the compression was released. The spinal fluid was clear, and no cells were found microscopically. The total protein was 16 mg per 100 cc, and the Wassermann test was negative.

On the tenth day the patient aspirated some milk that she was trying to drink. She rapidly became cyanotic and lost consciousness, and artificial respiration was instituted. The patient was

put into a respirator but did not regain consciousness. The temperature rose to 105.8°F, and the pulse to 160. After the administration of oxygen the cyanosis cleared slightly. Corneal reflexes were absent, and there was no response to painful stimuli. The eyes were partly open, and there was a bilateral twitching of the upper lids. The pupils were large and reacted slightly to light. There was little tone in the arms, but more in the flexors than in the extensors. The legs were flaccid. The biceps, triceps and knee jerks were extremely weak.

Three hours later convulsive movements of the fingers and arms developed, but they were never violent. The fundi were normal. The patient remained unchanged for six hours, when muscular twitchings increased. The pupils became smaller but still reacted to light. Prior to death, the respirations became shallow and infrequent and the patient seemed to be choking. She died twelve hours after the onset of the attack of respiratory difficulty.

DIFFERENTIAL DIAGNOSIS

DR ARTHUR WATKINS. This case seems to be one of a rather rapidly progressing neurologic disorder. Before discussing the nature of the pathologic process, I shall first try to localize it anatomically.

The chief complaint, and also the first complaint, was difficulty in speaking. This began five months before admission to the hospital and was a defect of articulation rather than any type of aphasia. One at once suspects some weakness of the vocal cords or palate, from a lesion of the tenth cranial nerve. We next learn that the patient salivated excessively, probably because of difficulty in swallowing, again on the basis of a palsy of the tenth cranial nerve. The fact that pills, probably atropine, did not relieve this is consistent. Three weeks before entry there was some diminution of vision, which might have been due to increased intracranial pressure, particularly so because the record states that she vomited without nausea, but since she had a headache only once, we cannot be sure of this. The vomiting may have been due to vertigo, since she felt dizzy while walking and was noted to have a staggering gait together with a "side-to-side movement" of the eyes, presumably nystagmus. I have already suggested a lesion of the tenth nerve to explain her speech and swallowing difficulties. A lesion of the ninth nerve could also make the gag reflex on swallowing difficult, and the symptoms of unsteady gait and nystagmus suggest involvement of the vestibular pathways from the eighth nerve or the descending cerebellar tract. From the history so far, we can suspect a lesion in the brain stem involving the nuclei of the eighth, ninth and tenth nerves. The acoustic portion of the eighth nerve seems to be eliminated through the absence of tinnitus and of diminution of hearing, and the history suggests no involvement of the extraocular muscles or of the long sensory and motor tracts.

The cerebral hemispheres seem to have been functioning, since she was able to maintain her school work.

Physical examination gave no indication of disease outside the central nervous system. Her voice was described as thick and nasal, suggesting that the speech defect was not in the loss of co-ordinated movement necessary for articulation, such as might result from a cerebellar or cerebral lesion, but due to weakness of the pharyngeal muscles. The extraocular movements were normal. The pupils were only slightly unequal in size, the right being smaller than the left, which makes one wonder about a beginning Horner's syndrome. There was some left facial weakness, indicating that the lesion might have been as high as the seventh cranial nerve. We have further evidence of dysfunction of the vestibular tract or of the connection between the vestibular nucleus and the cerebellum in the inaccurate finger-to-nose and heel-to-shin tests and the reeling gait with a tendency to fall to the left, the negative Romberg test showing that sensation in the extremities was normal.

We next find a suggestion of twelfth-nerve involvement in the weakness of tongue musculature, and that of the eleventh nerve in the weakness in flexion and rotation of the head and neck. The sensory and motor tracts of the extremities were apparently unaffected. The history and physical findings, therefore, lead us to suspect a lesion in the anterior portion of the brain stem affecting primarily the nuclei of the tenth nerve, with extension upward to the seventh and downward to the twelfth. While in the hospital, the patient developed respiratory paralysis, indicating involvement of the respiratory centers in the medulla, and finally died. She did lose consciousness but this seems likelier to have been due to respiratory difficulty or possibly an increase in intracranial pressure than to any primary involvement of the cerebrum. One might consider the possibility of a pseudobulbar palsy from a bilateral supranuclear lesion, but in the absence of pyramidal-tract signs this seems to be excluded.

Having decided that the lesion was localized to the brain stem, we shall now consider the nature of the lesion. We can first of all exclude an infectious process because of the absence of generalized signs of infection and because of the absence of meningeal signs and abnormalities in the cerebrospinal fluid. Degenerative conditions must then be considered. First of all comes bulbar palsy of the type associated with progressive muscular atrophy. The rapidity of the course and the absence of fibrillation of the tongue muscles or of the neck muscles make this extremely unlikely. Siringobulbia is another possibility, but again the course is too rapid and in this disease there are usually sensory symptoms through involvement of the spinal root of the fifth cranial nerve. In view of the nystagmus and difficulty in walking degeneration of the cerebellar

tract might be considered, such as Marie's ataxia, but the negative family history and the signs of cranial-nerve involvement easily exclude this diagnosis. An aneurysm may involve the upper cranial nerves, but it would not explain the sequence of events in this case. The steady progression of symptoms is against a vascular thrombosis.

We are left then with a diagnosis of tumor, which seems the most probable. The early involvement of the cranial nerves before long-tract signs and without much evidence of increase in intracranial pressure, favors a tumor arising within rather than outside the brain substance. This was probably a rapidly growing glioma, such as a spongioblastoma. Medulloblastoma might be thought of, particularly in this age group, but such a tumor is usually located in the fourth ventricle and cerebellum. There was probably a terminal pulmonary infection because of the difficulty in swallowing. My diagnosis therefore is glioma of the brain stem, with secondary bronchopneumonia.

CLINICAL DIAGNOSES

Bulbar palsy (cause unknown)
Aspiration asphyxia

DR WATKINS'S DIAGNOSES

Glioma of brain stem
Bronchopneumonia

ANATOMICAL DIAGNOSES

Glioblastoma multiforme of medulla
Asphyxia
Bronchopneumonia

PATHOLOGICAL DISCUSSION

DR CHARLES S KUBIK Postmortem examination revealed a large glioma of the medulla, involving the left half much more than the right. The tumor did not invade the pons. Histologically it was a glioblastoma multiforme, like most of the other gliomas of the brain stem that have been examined in this laboratory. There was early bronchopneumonia.

The terminal episode was unquestionably due to asphyxia resulting from aspiration of fluid. Before the air passages could be cleared, the brain had suffered such severe damage that the patient never regained consciousness. Hyperthermia, which occurred in this case, has been regularly observed after severe asphyxia resulting in a prolonged course or death.

An interesting and, in my experience, a unique feature was the lack of any paresthesia or sensory loss. It might be added that this was looked for with the greatest care on numerous occasions.

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CHRISTMAS 1945

CHRISTMAS, this year, will be celebrated with mixed emotions. War, as usual, has been immediately succeeded not by peace on earth and in the hearts of men, but by frustration, bitterness, suspicion and anxiety for the future. Wounds cannot heal so quickly, nor can scars be changed into normal tissue. We have, it is true, the happiness of many reunited families to give us joy, and the fact that the greater strife has ceased, we also have the recollection of those families that will never be reunited again, of the many thousands of physically and mentally crippled veterans who will continually challenge our right to the complacent en-

joyment of a re-established freedom, and of our lack, still, of the essential factor of good will among nations.

Since Christmas is the day of giving and receiving gifts, however, we are hoping for certain gifts this year—to be given and received by all—that have been missing since these troubled seasons began. They are not the gifts of soft living to replace hard living or of moral relaxation to replace moral vigor. They are rather those intellectual gifts that will enable their possessors to adapt themselves to their present without looking back too reluctantly on their past, that will guide them to the acceptance of a method of living and a manner of thought necessary for the future survival of the nations.

What the world is hungering for this Christmas is not a new mechanical toy or a more complicated piece of machinery than we have ever seen before, or a form of energy that will set a million men adrift upon a sea of idleness. It is not the product of mechanical minds that we now need, but a light to shine, as we must believe it will shine, to show us the way and give us the will for seeing and understanding each other's problems and each other's hopes.

It is not so much peace on earth and good will to men that we are wishing for this Christmas as it is good will among men in order that there may be peace on earth. Good will is not a product of the peace table or a handout of the politicians. It is a force that must come into the minds of each individual and be strengthened in the circle of each family, for inevitably the future of the world must depend on the will of those who inhabit it.

As Esaias the prophet once said, "The people which sat in darkness saw great light, and to them which sat in the region and shadow of death light is sprung up" — *Matthew* iv, 16.

INFLUENZA

BETWEEN 1920 and 1944, there were sixteen epidemics of influenza in the United States. At least six of them were nation wide, and the rest were

tract might be considered, such as Marie's ataxia, but the negative family history and the signs of cranial-nerve involvement easily exclude this diagnosis. An aneurysm may involve the upper cranial nerves, but it would not explain the sequence of events in this case. The steady progression of symptoms is against a vascular thrombosis.

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An interesting and, in my experience, a unique feature was the lack of any paresthesia or sensory loss. It might be added that this was looked for with the greatest care on numerous occasions.

always been accompanied by a sharp increase in mortality from pneumonia. It will be recalled that during the pandemic of 1918 the pneumonias that accompanied the influenza were of unusual severity and were associated with a high case fatality. Although the nature of the virus that probably was the causative agent of that pandemic is not known, bacteriologic studies of the pneumonias indicated that the bacteria varied in different localities: the influenza (Pfeiffer) bacillus, hemolytic streptococci, pneumococci and staphylococci were the predominant organisms. During an outbreak of influenza A virus infection in Boston in 1940-1941 there appeared to be an increase in the incidence of staphylococcal pneumonias⁴ and in the one of 1943-1944, an increase in the frequency and severity of pneumococcal pneumonias was noted.⁵ In 1940 the presence of influenza B virus infections was demonstrated during an epidemic of Type 1 pneumococcus pneumonia in a small community in upstate New York.³

Bacterial pneumonias have not been unusually severe or frequent since the influenza epidemic of 1943-1944. Should influenza spread in the community, there may be an increase in the incidence and severity of pneumonia during the early part of the present season, but effective agents are now available in the form of sulfonamides and penicillin. These must be used intelligently to yield the maximum benefit. The administration of occasional or subeffective doses of either of these agents as a preventive of pneumonia may give an unwarranted sense of security to both the patient and the physician and the application of effective full-dose therapy may thereby be delayed to a point at which it will be of no avail. When these agents are indicated they should be given intensively until their full effects are obtained. It is well to bear in mind that the pneumonias complicating influenza may be severe and fulminating in character. Some of them, to be sure, may be due to a pure virus infection and cannot be influenced by any specific treatment that is now available. On the other hand, most of them are bacterial complications of the primary viral infection and should be treated as such.

Repeated warnings have recently been given about an impending shortage of penicillin. This

is now real and present. Many large communities have been forced to ration penicillin informally, and controls on distribution by the Civilian Production Board are almost inevitable. It is well recognized by every physician that by far the greatest proportion of penicillin is prescribed for conditions in which no benefit can be expected; that dosages are excessive; that treatment is unnecessarily prolonged; and that amounts beyond all reason are wasted by oral administration. Should the influenza epidemic be complicated by staphylococcal pneumonias or by infections with hemolytic streptococci that are not susceptible to sulfonamides, a real danger exists that many persons will die because of an inadequate supply of penicillin for the treatment of these secondary infections, and this will be solely attributable to the wasteful and unwarranted use of penicillin in conditions in which it is not specifically indicated. The intelligent use of the supplies of penicillin currently made available, however, should guarantee an amount of the drug that will be more than ample to meet any emergency.

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MASSACHUSETTS MEDICAL SOCIETY DEATHS

CREGG — Francis A. Clegg, M.D. of Methuen, died November 30. He was in his sixty-fifth year.

Dr. Clegg received his degree from Jefferson Medical College of Philadelphia in 1905.

WHILE — Levi White, M.D. of Worcester, died December 1. He was in his ninety-seventh year.

Dr. White received his degree from Bellevue Hospital Medical College, New York, in 1872. At first he practiced in East Douglas and then in Milford, but in 1900 he moved to Worcester where he had continued in active practice until two years before his death. He was the oldest living member of the Massachusetts Medical Society.

His widow survives.

MISCELLANY

ADVISORY BOARD ON HEALTH SERVICES FOR RED CROSS

Basil O'Connor, national chairman of the American Red Cross, recently announced appointment of an Advisory Board on Health Services to co-ordinate activities of the American Red Cross in the health field. Mr. O'Connor

limited to various parts of the country. In each of the epidemics that occurred subsequent to 1932, the presence of influenza A or B virus was demonstrated either by serologic tests or by isolation from cases.

The last extensive epidemic occurred in the latter part of 1943 and early in 1944. In that epidemic, influenza A virus was isolated from cases in many widely separated areas throughout the United States and in Great Britain. The epidemiologic information concerning that epidemic indicates that it was of major proportions, the largest since that of 1928-1929. Although complications and case fatality rates in that outbreak were low, the effect of this epidemic on the total mortality, by virtue of the high incidence, was greater than the case fatality rate seemed to indicate.

During this epidemic, the Commission on Influenza of the United States Army made a fairly extensive study of the effect of vaccination with formalinized influenza A and B virus suspensions, concentrated from the allantoic fluid of infected chick embryos. A summary of the results was published last spring,¹ and the details of that study, which was made by several groups of workers in different parts of the United States, have been recently reported.² A definite reduction in the incidence of cases occurred in the vaccinated as compared with the control persons within the same groups. The ratio of the incidence of cases among controls to that among vaccinated subjects varied, in the experiences of different workers, from as little as 14:1 in California to as high as 60:1 in one group of subjects in New York City.

The full effectiveness of this method of vaccination, however, still remains to be demonstrated. Certainly little if any benefit can be expected from the vaccination of any group or community after an outbreak of influenza has already reached its

peak. Furthermore, since the immunity from vaccination probably does not persist for more than a few weeks or months, it must be undertaken somewhat in advance of the occurrence of an epidemic. Reactions to the injections of the vaccine, although not frequent, have nevertheless been observed and in some persons have been quite severe. Sensitization to egg protein is a possibility and may be quite a serious matter in persons with allergic tendencies. The last is equally true of vaccines used for im-

munization against viral or rickettsial diseases, most of which are prepared from infected eggs, and undoubtedly many of the troops who were vaccinated against yellow fever or typhus fever have been sensitized to egg protein. All such vaccines must therefore be administered under careful supervision and control.

According to news reports, a significant proportion of the personnel

of the United States Army who are still in active service have been injected with a vaccine similar to the one tested by the Commission on Influenza. There is no indication, however, that the other services have seen fit to follow this example. The supply of the vaccine has been limited, and little will be available for civilian use.

In recent weeks there has been evidence of outbreaks of influenza in various parts of Europe and on this continent. In each area where studies have been made, the presence of influenza B virus has been demonstrated. This is encouraging, for in the past, epidemics due to influenza B virus were neither so widespread nor so severe as those due to influenza A virus. Individual cases, however, have shown a similar variation in severity, regardless of the viral agent.

The Commission on Acute Respiratory Diseases of the United States Army and the New York State Department of Health³ have recently called attention to the fact that outbreaks of influenza have

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The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to

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PRIMARY ANASTOMOSIS IN CARCINOMA OF THE COLON*

HOWARD M. CLUTE, M.D.,† AND FRANCIS R. KENNEY, M.D.‡

BOSTON

THE changes in the surgical management of malignant lesions of the colon effected in the last few years have resulted in a marked reduction in the mortality following radical operations on the large bowel. It was our intention to study recent colon cases with particular emphasis on the part that chemotherapy had played in improving the results. It became increasingly apparent, however, that many factors other than chemotherapy were responsible for the progress made.

With the advent of chemotherapy and its application to various fields of surgery, the value of careful preoperative preparation, of meticulous surgical technic and of individualized postoperative care has faded in the light of general enthusiasm for the new drugs now at one's command. Increasing experience, however, is demonstrating that in the conditions in which operative measures are indicated the general surgical management of the patient is still of the greatest importance and that chemotherapeutic measures are only one part — and perhaps a relatively small part — of this management.

The present study covered 65 patients with cancer of the colon, including the rectosigmoid, operated on by one of us (H. M. C.) and Dr. Thomas J. Anglem from January 1, 1943, to April 1, 1945. Although this series is not a large one it has been of value in reviewing the results obtained with the new surgical approach of recent years.

No long discussion of our general preoperative measures is needed. It is believed, however, that increasing attention to the severe anemia that many patients have and its treatment by repeated transfusions, the study and management of their protein deficiencies and the generous use of blood transfusions before, during and after operation have contributed greatly to the results attained. In addition to blood, one of the intravenous amino acid

preparations has been employed, both preoperatively and postoperatively.

The methods we have used for the preparation of the colon in unobstructed cases have changed materially — and for the better. Drastic purgatives for two or three days before operation have been replaced with one or two cleansing enemas on the day of entrance, following which the colon is left alone. Most of the recent patients have been given sulfasuxidine in 2-gm. doses five times a day for three or four days before operation. There have been no toxic reactions from this drug. During this period the patient is given a high-calorie diet rich in proteins and carbohydrates and with slight residue. Clinical observations and the opinions of head nurses make it clear that the sulfasuxidine acts as a mild laxative as well as a means for reducing in some degree the bacterial flora of the gastrointestinal tract. Certainly the stools become mushy and soft and have little odor. Abdominal distention is decreased, especially in patients already partially obstructed. Regardless of the possible value of sulfasuxidine as a bactericide, it has proved to be a valuable agent simply for the preparation of the colon for surgery. It is logical, however, to believe that a drug that experimentally and clinically reduces the number of bacteria in the colon and has a very low rate of systemic reaction should be valuable in colonic surgery. That sulfasuxidine, however, is not the only factor in improving results is shown by the excellent results in these cases, in most of which the drug was not used.

Coller and Vaughan¹ have recently published their remarkable results in surgery of the colon, which was carried on largely without the use of sulfonamide drugs. Pemberton,² of the Mayo Clinic, on the other hand, reports equally good results in a large series of cases and believes that much of the improvement was directly related to the use of sulfonamides. The inference is clear that it is not a single factor that makes for better surgery in cancer of the colon but better general surgical management in all its details.

*Presented at a meeting of the New England Cancer Society, Boston, April 27, 1945.

†Surgeon, New England Baptist Hospital.

‡Assistant visiting surgeon, Massachusetts Memorial Hospitals.

named as board chairman Lewis H. Weed, M.D., of Baltimore, who is also chairman of the Division of Medical Sciences, National Research Council, and director of the School of Medicine, Johns Hopkins University.

The committee consists of one hundred and nine men and women from twenty-five states and the District of Columbia, representing every specialty in the field of health. Not only physicians were appointed, but also nurses, dentists, health educators, medical and psychiatric social workers, hospital administrators, medical publicists, nutritionists, pediatricians, public-health administrators and sanitary engineers.

The new group was appointed as a result of a recommendation made by the Special Medical and Health Survey Committee, which Mr. O'Connor named in October, 1944, to study Red Cross health programs and make recommendations. Other recommendations of the survey group, such as the Red Cross civilian blood-donor program, are already being carried out and still others are under consideration by the Red Cross central committee. The following departments are among those on whose programs the new board will advise: nutrition, nursing, home nursing, nurse aides, first aid, water safety and accident prevention, medical aspects of home service, hospital service, civilian relief, disaster relief, and canteen corps and nutrition aides.

COLONEL LANMAN AWARDED LEGION OF MERIT

Colonel Thomas Hinckley Lanman, M.C. A.U.S., on leave of absence as a member of the Surgical Staff of the Children's Hospital and as assistant professor of surgery at the Harvard Medical School, was recently awarded the Legion of Merit by direction of the President. The citation reads as follows:

For exceptionally meritorious service in the performance of outstanding service as surgical consultant for the 12th Hospital Center. Colonel Lanman displayed outstanding judgment, zeal, and devotion to duty in directing the surgical policies for the care of thousands of battle casualties. This has resulted in the saving of life in the prevention of serious complications and in shortening the time of incapacity.

CORRESPONDENCE

DEPRIVATION OF LICENSES

To the Editor: At a meeting of the Board of Registration in Medicine held November 30, the Board took the following actions:

To revoke the license of Dr. Lillian M. Lawford, 210 Maverick Street, East Boston, because of gross misconduct in the practice of her profession as shown by an illegal abortion.

To suspend for one year the license of Dr. John H. Walker, formerly of 665 Broad Street, Weymouth, and now of Rockland, Maine, because of gross misconduct in the practice of his profession as shown by violation of the federal narcotic law.

H. QUIMBY GALLUPE, M.D., Secretary
Board of Registration in Medicine

State House
Boston

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Constitution and Disease. Applied constitutional pathology. By Julius Bauer, M.D., professor of clinical medicine, College of Medical Evangelists, Los Angeles, senior attending physician, Los Angeles County General Hospital, and consultant

in medicine Cedars of Lebanon Hospital, Los Angeles. Second edition, revised and enlarged. 8°, cloth 247 pp. New York: Grune and Stratton, 1945. \$4.00.

The text in this new edition of a standard monograph, first published in 1942, has been amplified by the author and new citations covering the most recent literature have been added to the text, constituting a considerable addition to the bibliography of the subject.

NOTICES

ANNOUNCEMENTS

Dr. Edward A. Edwards, having recently returned from overseas duty with the Army, announces the reopening of his office at a new location, 29 Lewis Avenue, Great Barrington.

Dr. Laurence B. Ellis announces the reopening of his office at 319 Longwood Avenue, Boston, for the practice of internal medicine and cardiology.

Dr. Burton C. Grodberg, having returned from active service with the United States Army, announces the opening of his offices at 640 Main Street, Malden, and 353 Commonwealth Avenue, Boston, for the practice of obstetrics and gynecology.

Dr. Harold D. Levine, recently discharged from military service, announces the opening of his office at 171 Bay State Road, Boston, for the practice of internal medicine and cardiology.

Dr. Joseph Prehn announces the opening of his office at 483 Beacon Street, Boston, for the practice of ear, nose and throat.

NEW ENGLAND OTO-LARYNGOLOGICAL SOCIETY

The annual meeting of the New England Oto-laryngological Society will be held in conjunction with the American Laryngological, Rhinological and Otological Society, Incorporated, Eastern Section, at the Hotel Statler, Boston, on Wednesday, January 9, at 9:30 a.m.

The annual dinner of the Society will be held at the Harvard Club at 6:00 p.m. The guest speaker will be Dr. Julius Lempert, of New York City.

HELEN PUTNAM FELLOWSHIP

Radcliffe College invites application for the Helen Putnam Fellowship for Advanced Research in the general field of genetics or of mental health. The fellowship carrying a stipend of \$2000 and covering a period of eleven months, from October 1, 1946, is open to mature women scholars who have gained their doctorate or possess similar qualifications, and who have research in progress. All normal laboratory facilities will be provided to the winner of the Putnam Fellowship, whose appointment will be announced about May 1st by the Committee on award. Applications for the award must be submitted to Radcliffe College, Cambridge, Massachusetts, not later than April 1, 1946.

AMERICAN COLLEGE OF PHYSICIANS

The American College of Physicians will resume its annual meetings in 1946. The first postwar meeting will be held at the Philadelphia Municipal Auditorium from May 13 to 17 inclusive. The meeting will be conducted under the presidency of Dr. Ernest E. Irons, of Chicago, and the general chairmanship of Dr. George M. Piersol, of Philadelphia.

AMERICAN BOARD OF OPHTHALMOLOGY

The American Board of Ophthalmology announces the following examinations in 1946: Chicago, January 18-22, New York City, approximately April 10-13, San Francisco, June 22-25, and Chicago, October 9-12.

(Notices continued on page 79)

There were 6 cases of cancer of the transverse colon (Table 3). One was inoperable and only a cecostomy was done. In 5, the lesion was resectable. In 2 cases a primary resection and end-to-end suture without cecostomy were done, and in 3 a Mikulicz-type resection and later colostomy closure. In one of these 3 cases, a secondary closure of the colostomy became necessary after several weeks in the hospital. In another, reoperation for small-bowel obstruction was required — a total of eight operations and many applications of clamps to the colostomy spur in 3 cases. In the third case, the Mikulicz procedure was life-saving, the patient having had a resection of the right colon for cancer twelve years previously, but in the other two cases it is certain that a preliminary cecostomy could have been safely followed by an end-to-end suture. This, in the light of recent experience, would have been safer and better than the procedure adopted.

There were 6 cases of cancer of the splenic flexure (Table 4). A palliative operation was done in 3 of

TABLE 4 Treatment of Carcinoma of Splenic Flexure

TREATMENT	NO OF CASES	NO OF DEATHS	MORTALITY %
Palliative operation			
End-to-end suture colon, resection of spleen and part of stomach	1	0	0
Mikulicz resection of splenic flexure and part of ileum	1	1	100
Colo-colostomy	1	0	0
Totals	3	1	33
Average			
Resection			
End-to-end anastomosis	2	0	0
Resection of part of pancreas	1	0	0
Mikulicz operation	1	0	0
Colostomy closure			
Totals	3	0	0
Average			

these, in 2 of which it was an extensive and radical procedure. One of these patients died after a Mikulicz resection of the splenic colon and a resection of part of the ileum and a side-to-side anastomosis. It is to be noted, however, that in 1 case the colon was resected with an end-to-end anastomosis and that the spleen, along with part of the stomach, was also removed, with immediate normal recovery. In 2 of the remaining cases, the cancers

TABLE 5 Treatment of Carcinoma of the Descending Colon

TREATMENT	NO OF CASES	NO OF DEATHS	MORTALITY %
Resection			
End-to-end anastomosis	4	0	0
Resection of small bowel	1	0	0
Mikulicz operation	2	0	0
Preliminary cecostomy	3	0	0
Colostomy closure	0		
Totals	6	0	0
Average			

of the splenic flexure were resected and an end-to-end suture was carried out without difficulty. In the last case, a Mikulicz operation was done and the colostomy was later closed.

There were 6 cases of cancer of the descending colon — all resectable (Table 5). In 4 cases a resection and end-to-end suture were done, with no deaths. In 1 of these a piece of small bowel was also removed. In 2 cases, a Mikulicz resection was done. No attempt was made to close the colostomy of one of these patients because of age and disabilities, the second patient was a recent resection. We believe that today we could safely handle each case with a one-stage resection following preliminary cecostomy with a catheter.

Twenty-six patients had lesions in the sigmoid (Table 6). Seven cases were inoperable. Three of

TABLE 6 Treatment of Carcinoma of the Sigmoid

TREATMENT	NO OF CASES	NO OF DEATHS	MORTALITY %
Palliative operation			
Cecostomy	3	2	67
Colostomy	4	0	0
Totals	7	2	29
Average			
Resection			
End-to-end anastomosis	8	0	0
Preliminary cecostomy	3		
Mikulicz operation	11	2*	18
Preliminary cecostomy	1		
Colostomy closure	5		
Totals	19	2	11
Average			

*One of these patients died following closure of the colostomy apparently from coronary thrombosis.

these had a cecostomy only, and 2 of them died within hours or days of this procedure. In 4 cases, exploration and permanent colostomy was done, with no deaths. In the other 19 cases resection was done. In 8 of these, the operation was an end-to-end suture, with no deaths. Three of these patients had a preliminary cecostomy. It would probably have been safer to have done a preliminary cecostomy or at least a complementary one in all, although none of the patients without cecostomy caused any concern. This is the type of case in which Wangenstein suction seems especially valuable. The remaining 11 patients received Mikulicz resections, and 1 of these had a preliminary cecostomy. One patient died suddenly from a pulmonary embolus after the first-stage operation, having been up and about for five days. Five of these 11 patients have had their colostomies closed, and 1 of these 5 died after the second operation, apparently from a coronary thrombosis. Many Mikulicz resections of the sigmoid were done on feeble, elderly people or patients with liver metastases in whom it was not planned to close the colostomy. We now believe that it would render such patients a better service to do the resection in one stage, with an end-to-end suture and complementary cecostomy. With widening experience we shall probably be forced into fewer and fewer Mikulicz operations for removing cancers of the sigmoid.

Eleven patients had cancer of the rectosigmoid (Table 7). Five of these were inoperable, but in 6 it was possible to resect the lesion, with no deaths.

In our preoperative treatment, constant Wangenstein suction drainage of the stomach was used in almost every case, a practice recently recommended by Singleton et al.³ This was usually started the night before operation, and was always continued postoperatively until peristalsis had been re-established and the patient was passing gas by rectum. This maneuver has been of marked value in reducing postoperative complications and distress.³

All surgeons are strongly interested in the surgical technic best adapted for the removal of cancers of the colon. It is at once apparent from a study of our results and of the reports from most other clinics that there is no one plan of operation that is applicable to every lesion of the colon. This is true, first, because of the difference between the contents of the right colon and that of the left, second, because of the degree of obstruction and distention that usually accompanies the lesions, and finally, because of the varying degrees of operability. Relatively few surgeons now believe that all cancers of the colon, wherever situated and however complicated, are best handled by the same fundamental operative technic.

The ideal procedure appears to be wide removal of the tumor and its lymph node-bearing mesentery and immediate restoration of intestinal continuity. For this reason we have wherever possible refrained from resections of the Mikulicz or obstructive types and have instead used intestinal anastomoses, in either one or two stages. As the statistics show, this change has not increased the mortality rate. These figures do not, however, emphasize the gain in the patient's comfort and the decrease in trying procedures such as the repeated applications of clamps to Mikulicz spurs and the toilet of the colostomies—especially the ileocolic type—that accompany direct intestinal suture.

It seems evident, however, that there is a place for the Mikulicz type of operation, even though increasing experience indicates that it will be used less and less in the future. In the last two years we have used it primarily in the poor-risk cases with partial obstruction and some degree of infection, because it can be carried out quickly along with simultaneous decompression of the proximal bowel. The review of this series, however, strikingly demonstrates the relatively infrequent use of preliminary cecostomy in many of these patients. We believe that more frequent cecostomies will increase the opportunities to do direct intestinal anastomoses with safety and to reduce further the necessity of doing a Mikulicz operation in such cases.

* * *

In tabulating results the form used by Collier and Vaughan¹ has been followed, not only because it is extremely simple but also because it makes their

relatively large series of cases comparable with ours. The sites of the tumors are listed in Table 1.

TABLE 1 Site of Carcinoma of the Colon

SITE	No. of Cases
Right colon (cecum, ascending colon and hepatic flexure)	10
Transverse colon	6
Splenic flexure	6
Descending colon	6
Sigmoid	26
Rectosigmoid	11
Total	65

Ten patients had carcinoma of the right colon (Table 2). One of these was found on exploration

TABLE 2 Treatment of Carcinoma of the Right Colon.

TREATMENT	No. of Cases	No. of Deaths	MORTALITY %
Palliative operation			
Celiotomy	1	0	0
Totals	1	0	
Average			0
Resection			
One stage colectomy	1	0	0
Enterostomy	1		
Two-stage colectomy	7	1	14
Ileotransverse colostomy			
Mikulicz operation	1	0	0
Closure of colostomy			
Totals	9	1	
Average			11

to be inoperable. In the 9 other cases, the lesion was resectable. In 1 case this was safely done by a one-stage removal of the terminal ileum, cecum and ascending colon and part of the transverse colon. In 7 patients, the colectomy was done in two stages—first an ileocolostomy and later a resection of the right colon. One of these patients died of shock forty-eight hours after the second-stage operation, as a result of faulty surgical judgment in attempting it. This patient was sixty-six years of age and was short and fat, with a large diaphragmatic hernia and a seriously damaged heart. Better judgment would have classed the case as inoperable because

TABLE 3 Treatment of Carcinoma of the Transverse Colon

TREATMENT	No. of Cases	No. of Deaths	MORTALITY %
Palliative operation			
Cecostomy with pentoneal drainage	1	0	0
Totals	1	0	
Average			0
Resection			
End-to-end anastomosis	2	0	0
Mikulicz operation	3	0	0
Colostomy closure	1		
Second colostomy closure	1		
Small bowel obstruction			
Totals	5	0	
Average			0

of the patient's general condition. The patient receiving the Mikulicz procedure was a young man with a large, infected, partly obstructing tumor in the hepatic flexure. It is probable that today the procedure adopted would be decompression with a Miller-Abbott tube and a two-stage intestinal anastomosis and right-sided colectomy.

lous surgical technic and with individualized post-operative treatment, most patients having cancer of the colon can be safely operated on by resection of the lesion and intestinal anastomosis, and this is the method of choice

REFERENCES

- 1 Collier F A, and Vaughan H H Treatment of carcinoma of colon *Ann Surg* 121 395-411, 1945
- 2 Pemberton, J DeJ Discussion of Collier and Vaughan ¹
- 3 Singleton, A O Rogers, F and Houston, F G Problem of intestinal cases complicating abdominal surgery *Ann Surg* 115 921-934 1942

THIOURACIL AS A CAUSE OF NEUTROPENIA AND AGRANULOCYTOSIS*

MARK FALCON LESSES, M D,† AND SAMUEL L GARGILL, M D ‡

BOSTON

THIOURACIL is an effective agent in the treatment of toxic goiter,¹⁻³ but this effectiveness is frequently associated with toxic reactions of varying degrees of seriousness. The most important of these manifestations that have been reported are swelling of the submaxillary salivary gland, drug fever, dermatitis, jaundice, and neutropenia and agranulocytosis.^{4, 5} Although most of these complications are formidable, none except agranulocytosis have produced fatalities. The purpose of this study is to inquire further into the undesirable effects of thiouracil on the blood.

Sixty-two patients, all but 1 of whom had thyrotoxicosis, have been treated with thiouracil for varying periods of time. Four patients developed neutropenia or agranulocytosis, and in 1 of the cases death ensued. These cases will be described in detail because of the insight they give into the mechanism of the deleterious effect of thiouracil on hemopoiesis, especially with regard to the granulocytes.

CASE 1 F M, a 56-year old housewife, was admitted to the hospital on March 31, 1943, because of fatigue and nervousness of 7 months' duration and dyspnea, palpitation, tremors and weight loss in the preceding 3 months.

Physical examination revealed a hyperactive patient with staring eyes and flushed facies. The skin was moist and warm. There were fine tremors of the extended tongue and hands. The thyroid gland was diffusely enlarged to about twice its normal size. The blood pressure was 110/70. The basal metabolic rate on admission was +30 per cent. All other pertinent laboratory data were normal.

The patient was given 0.6 gm of thiouracil for 17 days, 0.5 gm for 6 days and 0.2 gm daily thereafter. The basal metabolic rate gradually fell to -2 per cent, and she was able to leave the hospital 26 days after entry.

The patient was thereafter observed at weekly intervals in the Endocrine Clinic, where the white-cell count, basal metabolic rate, weight and pertinent clinical features were noted. The giving of 0.2 gm of thiouracil daily was continued. Thirty days after the beginning of treatment, the basal metabolic rate was -9 per cent. By the end of 8 weeks, it had dropped to -19 per cent and puffiness of the eyelids had appeared. After 10 weeks, the basal metabolic rate was -19 per cent, the blood cholesterol was 328 mg per 100 cc, and there was increasing puffiness of the eyelids and face. After 12 weeks, the patient complained of irritability and sluggishness and showed marked facial puffiness, with a thick, dry skin. The basal metabolic rate was -24

per cent, and the blood cholesterol 367 mg per 100 cc. Thiouracil was stopped because of myxedema. The white-cell count throughout the first 3 months of treatment ranged between 6400 and 10,500, with abundant granulocytes always present.

Thiouracil was not administered for the next 4½ months. In this period, the basal metabolic rate rose to +9 per cent and mild symptoms of thyrotoxicosis gradually redeveloped. Thiouracil was resumed on October 15 in a dosage of 0.2 gm daily. After 2 weeks, the basal metabolic rate had dropped to -4 per cent and the thyrotoxic symptoms had disappeared, and after 4 weeks, it was -13 per cent. By the 11th week, the patient looked slightly myxedemic and had a basal metabolic rate of -19 per cent and a blood cholesterol of 312 mg per 100 cc. The dosage of thiouracil was accordingly reduced to 0.1 gm daily. After 20 days, the thiouracil was again stopped because of progressive signs and symptoms of myxedema. Three weeks later, the basal metabolic rate had risen to +3 per cent and the patient felt and looked well. When she had not taken thiouracil for 7 weeks, however, mild thyrotoxic symptoms again appeared, associated with a rise in the basal metabolic rate to +21 per cent.

A third course of thiouracil, 0.2 gm daily, was therefore begun on March 16, 1944, approximately 1 year after the initiation of treatment. On April 15, the basal metabolic rate was +13 per cent, and as the patient still showed mild signs and symptoms of thyrotoxicosis, the thiouracil was continued. The white-cell count at that time was 6500.

On the following day, the patient was fitted with new dentures and noted tenderness in the roof of the mouth. On April 17, a sore throat developed, followed by a chill and a rise in temperature to 103.5°F. Examination showed an acutely ill woman with flushed facies, coated tongue, large, reddened tonsils covered with a grayish exudate and tender, swollen lymph glands at the angles of the jaw. The white-cell count was 1000, with no granulocytes. Thiouracil was stopped and the patient was admitted to the hospital.

Treatment consisted of three blood transfusions, 5 gm of sodium sulfadiazine and 9 gm of sodium sulfamerazine intravenously, 270 cc of Pentacelotide intramuscularly, liver extract and 150,000 units of penicillin. Ulcerations developed in the throat and tonsils. The white-cell count ranged between 900 and 1650. The hemoglobin was 11.3 to 12.5 gm per 100 cc, and the red-cell count averaged 4,000,000. No polymorphonuclear cells appeared at any time, but on the day before death 1 myelocyte was seen in a count of 25 cells. Two sternal bone-marrow biopsies were done on the 2nd and 4th hospital days, both showed a hypoplastic marrow with granulocytic aplasia. The patient died suddenly on the 6th day.

Autopsy showed that the immediate cause of death was tracheal obstruction, caused by a gelatinous mucoid plug that started just below the vocal cords and extended deep into the bronchi, with almost complete occlusion. This obstruction produced widespread pulmonary atelectasis and congestion which in turn gave rise to marked dilation of the right side of the heart. The pharyngeal ulcers that had been noted clinically were filled with necrotic plugs containing large numbers of bacilli and cocci, without cellular reaction to the necrotic tissue. The thyroid gland was enlarged to about twice its normal size and contained a 6-mm nodule. Microscopically there was alveolar hyperplasia. The marrow in the femur was yellow and fatty, with only a few small islands

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§The bone-marrow studies in this case were carried out by Dr. Benjamin Alexander of the Hematology Clinic and Laboratory.

In 2 cases, resection and end-to-end suture were done. In an elderly man the rectosigmoid was opened and sutured following the removal of a malignant polyp. In 2 cases, an abdominoperineal re-

TABLE 7 *Treatment of Carcinoma of the Rectosigmoid*

TREATMENT	NO OF CASES	NO OF DEATHS	MORTALITY %
Palliative operation			
Colostomy	5	1	20
Preliminary cecostomy	1		
Totals	5	1	
Average			20
Resection			
End-to-end anastomosis	2	0	0
Colotomy and excision of polyp	1	0	0
Abdominoperineal operation (one-stage excision)	2	0	0
Preliminary cecostomy	1		
Posterior resection	1	0	0
Preliminary colostomy	1		
Totals	6	0	
Average			0

section of the lower sigmoid and rectum was done. In an extremely obese woman a preliminary colostomy and posterior resection of the rectum were performed. Anatomically the rectosigmoid is a fairly precise area, but at the operating table whether the site of the lesion is called "lower sigmoid," "rectosigmoid," or "high rectum" is often a matter of the surgeon's opinion. It may be that some cases classified as cancer of the rectosigmoid were in reality cancer of the sigmoid or even the rectum. In the 5 inoperable cases, only a colostomy

Five of these patients died, a mortality of 29 per cent. In 48 cases, the lesion was operable. Three of these patients died, a mortality of 6 per cent.

In all intestinal sutures some type of so-called "aseptic anastomosis" was used. Today, when there are so many methods and instruments for such a procedure, there seems relatively little excuse for employing an open anastomosis. Even if it were believed that the bowel contents could be sterilized by chemotherapy, we should still use some type of aseptic anastomosis. Our preference is naturally for the use of the Furniss clamp or our modification of it.

For sutures we use multiple, short, running sutures of nylon or silk, taking great pains to be sure that the blood supply is adequate at the ends of the bowel, and being careful not to disturb the blood supply when sewing up the mesentery.

We stopped clearing away fat tabs and epiploic appendages from the area of the suture line some years ago, and now sew completely through them or use them to turn over onto the suture line.

SUMMARY AND CONCLUSIONS

In this series of 48 cases of resectable cancer of the colon, intestinal anastomoses were done in 34—in 27 as primary operations and in 7 as secondary (right colon) procedures. One patient in this group died of shock after a second-stage right colectomy, a mortality of 3 per cent. Mikulicz resection was

TABLE 8 *Mortality Statistics in All Cases*

TYPE AND SITE OF OPERATION	NO OF CASES	NO OF DEATHS	MORTALITY %	CAUSE OF DEATH
Palliative operation				
Right colon	1	0	0	
Transverse colon	1	1	100	Obstruction and peritonitis
Splenic flexure	3	1	33	Peritonitis from leakage
Descending colon	0	0	0	
Sigmoid	7	2	29	Obstruction and peritonitis, pulmonary embolism
Rectosigmoid	5	1	20	
Totals	17	5		
Average			29	
Resection				
Right colon	9	1	11	Shock (bad judgment)
Transverse colon	5	0	0	
Splenic flexure	3	0	0	
Descending colon	6	0	0	
Sigmoid	19	2	11	Coronary thrombosis, pulmonary embolism
Rectosigmoid	6	0	0	
Totals	48	3		
Average			6	
Grand totals	65	8		
Grand average			12	

could be done because of the extent of the growth. One of these patients died the day after operation, apparently from a pulmonary embolus. In 1 case, a preliminary cecostomy was done because of obstruction.

* * *

The over-all mortality for the entire series of 65 cases was 12 per cent, 8 patients dying in the hospital (Table 8). In 17 cases, the lesion was inoperable and only palliative procedures were done.

done in 18 cases, with colostomy closure in 10. In 8 cases, the colostomies were not closed. Two patients died,—one of embolism and the other of thrombosis,—a mortality of 11 per cent.

We believe that the Mikulicz operation in cancer of the colon should be used only in cases in which it seems impossible to re-establish continuity of the intestine by direct intestinal anastomosis, or unwise to attempt it.

With careful preoperative preparation, including preliminary cecostomies as indicated, with meticu-

Table 2, the patient exhibited the usual lymphocytosis characteristic of hyperthyroidism. She tolerated the drug well until July 28, when a rise in temperature to 99.5°F occurred. Thiouracil was continued in the same dosage. On the next day, the temperature rose to 100.5°F and the patient com-

On July 10, 1.0 gm of thiouracil daily was begun. This was continued until July 20, when the dosage was reduced to 0.6 gm daily. On July 31, it was further reduced to 0.4 gm

TABLE 2 Hematologic Findings in Case 3

DATE	WHITE-GRAV- CELL COUNT	DIFFERENTIAL COUNT	HEMO- GLOBIN	RED CELL COUNT	REMARKS
		N L M E			
		% % % %	%		
1944					
7-19	11,100	7 550	68 27 5 2	76	B M R. + 35% Thiouracil 1.0 gm daily begun
7-21	6,150	3 320	74 40 4 2		B M R. + 27%
7-22	6,250				
7-24	9,400	5 260	56 55 7 2		
7-25	7,800	4 300	55 40 5 0		
7-26	10,100				
7-27	10,600	6 675	63 25 9 3		
7-29	4,800	2,930	61 23 10 6		Fever up to 100.5°F Thiouracil omitted
7-30	5,100	2,450	48 40 9 3		B M R. + 13%
8-1	5,000	1,700	34 49 6 11		
8-2	7,900	3,560	45 45 8 4		
8-3	6,100	2,900	48 37 11 4		
8-4	7,900	4,070	51 38 10 1		

plained of a sore throat. Examination showed injection of the posterior pharyngeal wall and a white-cell count of 4800, contrasted with one of 10,600 on the previous day. The percentage of neutrophils had not changed. On July 30, the patient complained of sore throat and chilly sensations. Examination of the blood showed moderate leukopenia and beginning neutropenia. Thiouracil was stopped. On the next day, the temperature rose to 100°F and the patient complained of malaise and headache. On August 1, she was afebrile and symptom-free, but the blood examination showed persistence of the neutropenia and a moderate eosinophilia. Following this there was gradual improvement in the blood picture, so that on August 4 the white-cell count and the percentage of neutrophils approached those found prior to the administration of thiouracil.

The final basal metabolic rate on August 2 was +13 per cent. Administration of 10 drops daily of saturated solution of potassium iodide was begun on that day, and the patient was discharged home on August 5.

Comment. This patient with diffuse toxic goiter was treated with 1.0 gm of thiouracil daily for 7 days, when she developed a toxic reaction manifested by sore throat, fever and granulocytopenia. Stopping of the drug was followed by prompt recovery without further treatment. The patient exhibited the lymphocytosis associated with toxic goiter and had an average neutrophil count of 5400 before the toxic reaction. Following clinical recovery from this reaction, the neutrophils remained at the comparatively low level of 3500. At the height of the toxic reaction, the count dropped to 1700. Significant eosinophilia developed during recovery.

CASE 4. E. G., a 33-year old housewife, entered the hospital on June 26, 1944, complaining of irritability and easy fatigue. There had been a weight loss of 20 pounds in the preceding 9 months, and a goiter had appeared 6 months previously. There had also been increased appetite, hyperhidrosis, palpitation and decreased tolerance to heat.

On examination the patient was restless. There was moderate exophthalmos and slight puffiness of the eyelids. The skin was flushed, warm and moist. The thyroid gland was diffusely enlarged to five times its normal size and exhibited a loud bruit and widespread thrill. There were fine tremors of the tongue and hands. The heart was not enlarged, its rhythm was regular at a rate of 134, and there were no murmurs. The blood pressure was 140/70. Urine examination revealed no abnormalities. The initial and subsequent hematologic findings are given in Table 3. The fasting blood cholesterol was 141 mg per 100 cc, and the nonprotein nitrogen 29 mg. The icterus index was 6. The initial basal metabolic rate was +43 per cent.

The beginning treatment consisted of bed rest, a high-calorie diet and small doses of phenobarbital. Within a few days there appeared an erythematous maculopapular rash, which was interpreted as due to the phenobarbital. The drug was omitted and the rash disappeared after 4 days.

TABLE 3 Hematologic Findings in Case 4

DATE	WHITE-GRAV- CELL COUNT	DIFFERENTIAL COUNT	HEMO- GLOBIN	RED- CELL COUNT	REMARKS
		N L M E			
		% % % %	%		
1944					
6-26	5,100		88		
7-6	7,600	500	90		
7-11	7,000	46 44 10 0			
7-12	8,100	4 550	56 39 4 1		
7-13	5,000				
7-14	6,400	4 355	68 25 6 1		
7-15	7,700				
7-17	12,000	9 500	79 14 5 2		B M R. + 32%
7-18	4,600	3 050	67 25 6 2		
7-19	7,100				
7-20	6,200				Thiouracil 0.6 gm
7-21	9,000	5,500	62 30 1 2		
7-22	6,200				
7-24	4,200	3 280	78 22 0 0		B M R. + 26%
7-25	5,200	3 900	75 22 2 1		
7-26	6,500				
7-27	4,800	3 650	76 17 3 4		
7-28	4,000	2 850	72 24 2 2		
7-29	4,200	2 900	69 25 2 4		B M R. + 14%
7-31a	5,000	1 860	62 30 5 3		Temperature 99.4°F sore throat thioura- cil 0.3 gm
8-1a	5,450	1 415	41 43 9 6		Temperature 100°F thioura- cil omitted
8-1a	4,000	1 760	44 44 10 2		Temperature 99°F
8-2a	4,600	1 840	40 50 8 1		
8-3	4,100	1 270	31 48 1 12		
8-3	4,700	2 780	59 32 6 3		Normal tempera- ture
8-18	14,900	11 600	78 14 5 3		

By then, the basal metabolic rate had dropped to +14 per cent. As shown in Table 3, the patient had had leukopenia for several days. On August 1, the temperature rose to 100.5°F, there was a slight sore throat and further leukopenia and neutropenia were evident. Thiouracil was stopped, but there was no further therapy of the granulocytopenia. The blood picture gradually returned to normal. A saturated solution of potassium iodide was given for the treatment of the thyrotoxicosis. The patient was discharged on August 4 and was followed in the Endocrine Clinic.

Comment. This thyrotoxic patient received 1.0 gm of thiouracil daily for 10 days, 0.6 gm daily for the following 10 days and 0.4 gm daily for the next 2 days, when the drug was stopped because of sore throat, fever and granulocytopenia. Clinical and hematologic improvement rapidly ensued. At the height of the toxic reaction, the patient looked and felt well. The neutrophil count averaged 4275 before the toxic reaction and dropped to 1270 at the height of the reaction. It is significant that the number of granulocytes dropped well below the average level 3 days before fever and sore throat appeared. As in Case 3, marked eosinophilia signaled recovery. Moreover, as can be seen in Table 3, this patient exhibited the usual lymphocytosis of hyperthyroidism. Control of the thyrotoxicosis manifested itself by a normal neutrophil-lymphocyte ratio. With the development of toxic neutropenia there was reversion to the original neutrophil-lymphocyte ratio, but with an abnormally low number of granulocytes. The latter finding and the associated clinical phenomena of pharyngitis and fever adequately established the diagnosis of thiouracil neutropenia.

CASE 5. A. M., a 52-year-old housewife, entered the hospital on November 3, 1944 with the complaints of nervousness, thermophobia, hyperhidrosis, tremor of the hands and palpitation. There had been a weight loss of 14 pounds and a scanty menstrual flow during the preceding 9 months.

Examination showed restlessness, a flushed, warm, moist skin, lustrous, staring eyes without exophthalmos or lid lag, diffuse enlargement of the thyroid gland to twice its normal size, a slight basal and apical systolic murmur, without heart enlargement, a blood pressure of 140/70, and fine rapid tremors of the hands. Urinalysis showed no abnormalities. Detailed hematologic observations were made and are pre-

of marrow cells. In the vertebrae, sternum and ribs the marrow was abundant, pasty and slightly brownish. Sections from the ribs were at least half fat, the remainder consisted of marrow-forming cells, composed of an equal mixture of large, undifferentiated cells with a bluish cytoplasm and of normoblasts. No eosinophilic myelocytes were present.

Summary. This patient with toxic goiter received three courses of thiouracil during a period of 1 year. The first course of thiouracil with an average daily dose of 0.2 gm. lasted 3 months and was followed by myxedema and a remission of 4½ months' duration. The second course, also with an average daily dose of 0.2 gm., lasted for 14 weeks and was followed by the reappearance of myxedema and a remission lasting for 7 weeks. In the third and final course, the patient received a daily dose of 0.2 gm. of thiouracil for 4 weeks, at the end of which agranulocytosis suddenly appeared, followed by death in 6 days. Post-mortem examination showed extensive granulocytic hypoplasia of the marrow, ulcerative pharyngitis, an occluding tracheobronchial mucus plug, pulmonary congestion and atelectasis and acute dilatation of the right auricle and ventricle. The thyroid gland showed alveolar hyperplasia and hydropic degeneration, with the absence of colloid and of lymphocytic infiltration.

CASE 2. H. S., a 57-year old upholsterer, entered the hospital on September 3, 1942, because of severe angina pectoris and heart failure. He had been admitted 4 months previously for congestive heart failure.

Examination showed dyspnea, orthopnea and cyanosis and engorged neck veins. The heart was enlarged downward and to the left and had a loud systolic murmur at the mitral area. Both lung bases showed numerous moist rales. The liver was enlarged to 4 fingerbreadths below the right costal margin. Ascites and moderate ankle edema were present. The blood pressure was 140/110. Urinalyses showed specific gravities ranging between 1.010 and 1.020, a +++ test for albumin, no sugar and varying numbers of red and white cells, with occasional hyaline and granular casts in the sediment. The blood nonprotein nitrogen varied between 45 and 64 mg. per 100 cc. The blood carbon dioxide combining power was 46 vol. per cent. Numerous electrocardiograms showed a normal rhythm, with defective intraventricular conduction, left-axis deviation and prominent Q waves in Leads 1, 2 and 3. The hemoglobin was 110 per cent (16.0 gm.), the red-cell count was 5,600,000, and the white-cell count was 7900, with 64 per cent neutrophils, 34 per cent lymphocytes and 2 per cent monocytes. Roentgenography showed a hypertensive heart with marked pulmonary congestion.

The patient was treated with bed rest, salt restriction, digitalis, mercurial diuretics and nitroglycerin, but this regime failed to benefit the angina pectoris or establish cardiac compensation. Total thyroidectomy was considered, but was not undertaken because of impaired renal function. An attempt to produce myxedema by the use of thiouracil was therefore substituted. The basal metabolic rate in a series of five determinations ranged between +9 and +19 per cent. This elevation was attributed to heart failure, since the blood velocity (arm to tongue) was prolonged to 35 seconds and the venous pressure increased to 15 cm. of water.

On September 25, 1942, thiouracil was begun in doses of 0.8 gm. daily. At that time the red-cell count was 5,150,000, the hemoglobin 112 per cent (16.2 gm.), and the white-cell count 8000, with 75 per cent neutrophils, 23 per cent lymphocytes and 2 per cent monocytes. After 7 days the dosage of thiouracil was reduced to 0.6 gm. At that time, the hemoglobin was 114 per cent (16.5 gm.), the red-cell count was 5,900,000, and the white-cell count was 9300, with 61 per cent neutrophils, 31 per cent lymphocytes, 3 per cent monocytes, 4 per cent eosinophils and 1 per cent basophils. After 18 days, the thiouracil dosage was reduced to 0.4 gm. daily because on the preceding day the leukocytes had numbered 3300, with only 32 per cent neutrophils. The hemoglobin was 104 per cent (15.1 gm.) and the red-cell count 5,250,000.

Leukopenia continued despite the reduction of dosage, and 3 days later the white-cell count was 2100, with 7 per cent neutrophils, the hemoglobin had fallen to 90 per cent (13.1 gm.) and the red-cell count to 4,000,000. Thiouracil was stopped, and the patient was transfused with 750 cc. of whole blood and given 40 cc. of Pentnucleotide daily. On the following day, the white-cell count was 3300, with 11 per cent neutrophils. Thereafter the granulocytes increased steadily

in percentage and in total numbers, so that by the end of 6 days the white-cell count was 6700, with 64 per cent neutrophils (Table 1). During the period of neutropenia, the patient

TABLE 1 Hematologic Findings in Case 2

DATE	WHITE-CELL COUNT	GRANULOCYTE COUNT	DIFFERENTIAL COUNT					HEMOGLOBIN*	RED-CELL COUNT	REMARKS
			N	L	M	E	B	%		
			%	%	%	%	%	%		
1942									x10 ⁶	
9-20	7,900	5,050	64	34	2	0	0	110	5.6	Thiouracil, 0.8 gm. daily, begun 9-25
9-26	8,000	6,000	75	23	2	0	0	112	5.2	
10-1	9,300	5,675	61	31	3	4	1	114	5.9	Thiouracil reduced to 0.6 gm. daily
10-19	3,300	1,060	32	50	17	0	1	104	5.3	Thiouracil reduced to 0.4 gm. daily
10-20								106	5.3	Urticarial dermatitis thiouracil omitted
10-21	2,100	147	7	72	21	0	0	92	4.0	500 cc. whole blood
10-22	3,300	363	11	68	20	0	0			40 cc. Pentnucleotide
10-23	3,800	1,370	36	54	10	0	0			250 cc. whole blood
10-24	5,300	3,180	60	35	5	0	0			40 cc. Pentnucleotide
10-25	3,700	1,590	43	46	10	0	1	90	4.7	
10-26	6,700	4,290	64	29	7	0	0			
10-27	8,300	5,320	64	29	6	0	1			

*In this and subsequent tables 100 per cent hemoglobin is considered to be equivalent to 14.5 gm. per 100 cc.

had a single rise in temperature to 101.4°F and developed an urticarial dermatitis. The basal metabolic rate was not decreased as a result of the administration of thiouracil.

The patient was discharged on October 31, but was readmitted on February 10, 1943, because of recurrence of heart failure and died on April 29.

Autopsy showed aneurysm of the left ventricle, coronary sclerosis, left-ventricular hypertrophy, bronchopneumonia, bronchiectasis, a bronchiectatic cavity with small lung abscesses, chronic glomerulonephritis and chronic passive congestion. The thyroid gland was normal on gross and microscopic examination. The bone marrow was also normal, with active formation of both red and white blood cells.

Comment. In this patient with chronic heart failure and angina pectoris, the production of myxedema was attempted through the administration of thiouracil—0.8 gm. daily for 6 days, 0.6 gm. daily for 18 days and 0.4 gm. daily for 2 days. On the 25th day leukopenia and neutropenia were noted, and on the 27th day there was severe neutropenia, associated with a slight reduction in the hemoglobin level and the red-cell count. Simultaneously with the onset of the neutropenia, an urticarial dermatitis appeared. Complete temporary recovery ensued following stoppage of the drug and treatment with transfusions and Pentnucleotide.

CASE 3. L. C., a 34-year-old, unmarried woman, an office worker, entered the hospital on July 19, 1944, because of tremors of the hands, irritability, palpitation, increasing appetite and a weight loss of 15 pounds during the preceding 3 weeks. Staring of the eyes, excessive perspiration, fatigability and swelling of the neck had also been observed for 6 months, menstruation had been scanty but regular. A brother had undergone thyroidectomy for toxic goiter.

Physical examination disclosed a thin, overactive, apprehensive and trembling young woman with stary eyes. The skin was moist, flushed and warm. The thyroid gland was diffusely enlarged to twice its normal size. The heart showed a moderate systolic murmur, maximal at the pulmonic area and extensively transmitted over the precordium. The heart rate was 120, the rhythm was regular, and the blood pressure was 124/76. There was a fine tremor in the hands and legs. Urinalysis showed no abnormalities. The hemoglobin was 76 per cent (11.0 gm.), the red-cell count 3,720,000, and the white-cell count 11,100, with 68 per cent neutrophils, 27 per cent lymphocytes, 5 per cent monocytes and 2 per cent eosinophils. The blood cholesterol was 145 mg. per 100 cc., and the icterus index 6. The basal metabolic rate on July 19 was +35 per cent and on July 20 was +27 per cent. Thiouracil, 1.0 gm. daily, was begun on July 21. Daily white-cell and differential counts were made. As shown in

Table 2, the patient exhibited the usual lymphocytosis characteristic of hyperthyroidism. She tolerated the drug well until July 28, when a rise in temperature to 99.5°F occurred. Thiouracil was continued in the same dosage. On the next day, the temperature rose to 100.5°F and the patient com-

TABLE 2 Hematologic Findings in Case 3

DATE	WHITE-CELL COUNT	GRANULOCYTE COUNT	DIFFERENTIAL COUNT	HEMOGLOBIN	RED-CELL COUNT	REMARKS
			N L M E	%		
			% % % %			
1944						
7-19	11,100	7,550	68 27 5 2	76	3.7	B.M.R. + 35% Thiouracil 10 gm daily, begun 7-21
7-21	6,150	3,320	54 40 4 2			B.M.R. + 27%
7-22	6,250					
7-24	9,400	5,260	56 35 7 2			
7-25	7,800	4,300	55 40 5 0			
7-26	10,100					
7-27	10,600	6,675	63 25 9 3			
7-29	4,800	2,950	61 23 10 6			Fever up to 100.5°F Thiouracil omitted
7-30	5,100	2,450	48 40 9 3			B.M.R. + 13%
8-1	5,000	1,700	34 49 6 11			
8-2	7,900	3,560	45 43 8 4			
8-3	6,100	2,950	48 37 11 4			
8-4	7,900	4,050	51 38 10 1			

plained of a sore throat. Examination showed injection of the posterior pharyngeal wall and a white-cell count of 4800, contrasted with one of 10,600 on the previous day. The percentage of neutrophils had not changed. On July 30, the patient complained of sore throat and chilly sensations. Examination of the blood showed moderate leukopenia and beginning neutropenia. Thiouracil was stopped. On the next day, the temperature rose to 100°F and the patient complained of malaise and headache. On August 1, she was afebrile and symptom-free, but the blood examination showed persistence of the neutropenia and a moderate eosinophilia. Following this there was gradual improvement in the blood picture, so that on August 4 the white-cell count and the percentage of neutrophils approached those found prior to the administration of thiouracil.

The final basal metabolic rate on August 2 was +13 per cent. Administration of 10 drops daily of saturated solution of potassium iodide was begun on that day, and the patient was discharged home on August 5.

Comment. This patient with diffuse toxic goiter was treated with 10 gm of thiouracil daily for 7 days, when she developed a toxic reaction manifested by sore throat, fever and granulocytopenia. Stopping of the drug was followed by prompt recovery without further treatment. The patient exhibited the lymphocytosis associated with toxic goiter and had an average neutrophil count of 5400 before the toxic reaction. Following clinical recovery from this reaction, the neutrophils remained at the comparatively low level of 3500. At the height of the toxic reaction, the count dropped to 1700. Significant eosinophilia developed during recovery.

CASE 4. E. G., a 33-year old housewife, entered the hospital on June 26, 1944, complaining of irritability and easy fatigue. There had been a weight loss of 20 pounds in the preceding 9 months, and a goiter had appeared 6 months previously. There had also been increased appetite, hyperhidrosis, palpitation and decreased tolerance to heat.

On examination the patient was restless. There was moderate exophthalmos and slight puffiness of the eyelids. The skin was flushed, warm and moist. The thyroid gland was diffusely enlarged to five times its normal size and exhibited a loud bruit and widespread thrill. There were fine tremors of the tongue and hands. The heart was not enlarged, its rhythm was regular at a rate of 154, and there were no murmurs. The blood pressure was 140/70. Urine examination revealed no abnormalities. The initial and subsequent hematologic findings are given in Table 3. The fasting blood cholesterol was 141 mg per 100 cc., and the nonprotein nitrogen 29 mg. The icterus index was 6. The initial basal metabolic rate was +43 per cent.

The beginning treatment consisted of bed rest, a high-calorie diet and small doses of phenobarbital. Within a few days there appeared an erythematous maculopapular rash, which was interpreted as due to the phenobarbital. The drug was stopped and the rash disappeared after 4 days.

On July 10, 10 gm of thiouracil daily was begun. This was continued until July 20, when the dosage was reduced to 0.6 gm daily. On July 31, it was further reduced to 0.4 gm daily.

TABLE 3 Hematologic Findings in Case 4

DATE	WHITE-CELL COUNT	GRANULOCYTE COUNT	DIFFERENTIAL COUNT	HEMOGLOBIN	RED-CELL COUNT	REMARKS
			N L M E	%		
			% % % %			
1944						
6-26	5,100			88	4.3	B.M.R. + 43%
7-6	7,600	3,500	46 44 10 0	90	4.9	B.M.R. + 37%
7-11	7,000					Thiouracil 10 gm daily begun 7-10
7-12	8,100	4,550	56 39 4 1			
7-13	5,000					
7-14	6,400	4,355	68 25 6 1			
7-15	7,000					
7-17	12,000	9,500	79 14 5 2			B.M.R. + 32%
7-18	4,600	3,080	67 25 6 2			
7-19	7,100					
7-20	6,200					Thiouracil 0.6 gm
7-21	9,000	5,580	62 30 1 2			
7-22	6,200					
7-24	4,200	3,250	78 22 0 0			B.M.R. + 26%
7-25	5,200	3,900	75 22 2 1			
7-26	6,500					
7-27	4,500	3,650	76 17 3 4			
7-28	4,000	2,880	72 24 2 2			
7-29	4,200	2,900	69 25 2 4			B.M.R. + 14%
7-31 a.m.	3,000	1,860	62 30 5 3			Temperature 99.4°F sore throat thiouracil 0.3 gm
p.m.	3,600					Temperature 100°F thiouracil omitted
8-1 a.m.	3,450	1,415	41 43 9 6			Temperature 99°F
p.m.	4,000	1,760	44 44 10 2			Temperature 100°F thiouracil omitted
8-2 a.m.	4,600	1,840	40 50 8 1			Temperature 99°F
p.m.	4,100	1,270	31 48 1 12			
8-3	4,700	2,780	59 32 6 3			Normal temperature
8-18	14,900	11,600	78 14 5 3			

By then, the basal metabolic rate had dropped to +14 per cent. As shown in Table 3, the patient had had leukopenia for several days. On August 1, the temperature rose to 100.5°F, there was a slight sore throat and further leukopenia and neutropenia were evident. Thiouracil was stopped, but there was no further therapy of the granulocytopenia. The blood picture gradually returned to normal. A saturated solution of potassium iodide was given for the treatment of the thyrotoxicosis. The patient was discharged on August 4 and was followed in the Endocrine Clinic.

Comment. This thyrotoxic patient received 10 gm of thiouracil daily for 10 days, 0.6 gm daily for the following 10 days and 0.4 gm daily for the next 2 days, when the drug was stopped because of sore throat, fever and granulocytopenia. Clinical and hematologic improvement rapidly ensued. At the height of the toxic reaction, the patient looked and felt well. The neutrophil count averaged 4275 before the toxic reaction and dropped to 1270 at the height of the reaction. It is significant that the number of granulocytes dropped well below the average level 5 days before fever and sore throat appeared. As in Case 3, marked eosinophilia signaled recovery. Moreover, as can be seen in Table 3, this patient exhibited the usual lymphocytosis of hyperthyroidism. Control of the thyrotoxicosis manifested itself by a normal neutrophil-lymphocyte ratio. With the development of toxic neutropenia there was reversion to the original neutrophil-lymphocyte ratio, but with an abnormally low number of granulocytes. The latter finding and the associated clinical phenomena of pharyngitis and fever adequately established the diagnosis of thiouracil neutropenia.

CASE 5. A. M., a 32-year-old housewife, entered the hospital on November 3, 1944 with the complaints of nervousness, thermophobia, hyperhidrosis, tremor of the hands and palpitation. There had been a weight loss of 14 pounds and a scanty menstrual flow during the preceding 9 months.

Examination showed restlessness, a flushed, warm, moist skin, lustrous, staring eyes without exophthalmos or lid lag, diffuse enlargement of the thyroid gland to twice its normal size, a slight basal and apical systolic murmur, without heart enlargement, a blood pressure of 140/70, and fine rapid tremors of the hands. Urinalysis showed no abnormalities. Detailed hematologic observations were made and are pre-

sented in Table 4. The fasting blood sugar was 83 mg per 100 cc and the cholesterol 162 mg. The icterus index was 6. The basal metabolic rate before treatment varied between +19 and +29 per cent.

Thiouracil in daily doses of 1.0 gm was begun on November 9, and was continued at that level until November 12, when the dosage was reduced to 0.8 gm. This amount was ad-

TABLE 4 Hematologic Findings in Case 5

DATE	WHITE CELL COUNT	GRANULOCYTE COUNT	DIFFERENTIAL COUNT					HEMOGLOBIN	RED CELL COUNT	REMARKS
			N	L	M	E	%	%		
1944										
11-3	6,000	4,560	76	16	8			90	4.9	B M R. +29%
11-10	6,000	3,660	61	25	10	4		94	5.5	B M R. +17% on 2nd day of thiouracil, 10 gm. daily
11-11	4,950	3,620	73	18	8					
11-12	6,400	4,550	71	21	6	2				Thiouracil re- duced to 0.8 gm daily
11-14	5,650	4,180	74	19	3	4				B M R. +6%
11-15	5,100	3,820	75	17	4	4			3.9	
11-16 a m	4,000	2,320	58	32	2	7		84		B M R. +1%
11-16 p m	5,100									
11-17 a m	4,100	3,080	75	20	2	3		84	4.5	
11-17 p m	4,400									
11-18	4,500	3,600	80	15	2	3				B M R. -3%
11-19	3,950	2,840	72	18	7	3				
11-20	4,700	3,380	72	22	5	1				
11-21	5,500	3,850	70	22	3	5				
11-22	6,100	4,950	81	12	2	5				B M R. -6%
11-23	6,350	4,700	79	16	2	3				
11-24	4,900	3,820	78	18	1	3				
11-25	5,700	4,275	75	20	2	3				B M R. -6%
11-26	6,400									Thiouracil omitted
12-8	7,100	5,850	83	15	1	1		77	4.1	

ministered until November 26, when the patient was discharged. Thereafter, she took 10 drops of saturated solution potassium iodide daily. The response to thiouracil was prompt. At the end of 4 days of its administration, the basal metabolic rate had dropped to +6 per cent and there was marked clinical improvement. By the 10th day, it had dropped to -6 per cent, and it remained at that level until discharge. This remission has been further maintained by iodide medication.

Daily white-cell and differential counts were made during the administration of thiouracil to detect early toxic effects on the bone marrow. These are reported in Table 4.

Comment. This case is included to illustrate a benign hematologic reaction to the administration of thiouracil, characterized by slight leukopenia and neutropenia, with complete recovery in spite of continued administration of thiouracil.

DISCUSSION

In early animal investigations of the sulfur-containing compounds that simultaneously produce thyroid hyperplasia and inhibit hormone production, no reference is made to effects on hemopoiesis.⁶⁻⁸ When thiouracil and thiourea were utilized in the treatment of patients with toxic goiter, neutropenia and agranulocytosis appeared among the first toxic manifestations.¹⁻³ This effect was at first ascribed to overdosage or idiosyncrasy, but subsequent experience indicates that the etiologic mechanism of the hemopoietic depression is far from clear.

Astwood⁴ has reported 1 case of agranulocytosis and 1 case of marked leukopenia among 62 cases treated with thiouracil. The agranulocytosis in the first case was ascribed to the excessive dose of 2.0 gm daily. In the second case, which resembled Case 2, a patient with heart disease without thyrotoxicosis received 0.6 gm of thiouracil for sixty-two days and 0.3 gm for thirty-one days. On the

eighty-fifth day, sulfamerazine was given for a streptococcal infection of the finger, and by the ninetyeth day the granulocyte count had dropped to 100, with a white-cell count of 2000. Coincidentally, ulcerative stomatitis and pharyngitis developed. Recovery occurred after ten days. Despite the use of sulfamerazine, thiouracil seems implicated as the probable etiologic agent in this case because of the rarity of neutropenia during the first week of sulfonamide therapy. Although at first emphasizing the dosage factor in the causation of thiouracil neutropenia, Astwood has more recently raised the question of hypersensitivity tending to occur in allergic subjects.

Williams and Clute,³ in reviewing their experience with 72 cases of thyrotoxicosis treated with thiouracil, report 1 case of agranulocytosis and 1 case of neutropenia. In the latter case, the granulocyte count was 640 and the white-cell count 3200. Administration of thiouracil was continued, and the numbers of granulocytes and white cells returned to normal. These authors noted other mild leukopenic reactions, which they explained as part of the thyrotoxic syndrome, unrelated to the administration of thiouracil. In subsequent metabolic studies, Williams and his co-workers⁹ found the human bone marrow to be one of the tissues most highly saturated with the drug. They also found the concentration of thiouracil in white cells to be greater than that in red cells.

Gabrilove and Kert¹⁰ observed 1 case of neutropenia in 9 patients treated with thiouracil. The granulocyte count dropped from an initial level of 3420 to 1520 after 1 gm of thiouracil had been given for sixteen days, when the drug was stopped.

Paschkis and his co-workers¹¹ used thiouracil in the treatment of 17 cases of thyrotoxicosis and observed 1 case of leukopenia, with a white-cell count of 2500, after eight months of treatment with 1.0 gm of thiouracil daily. The count returned to normal within three days after stoppage of the drug, and was again depressed within forty-eight hours after resumption of treatment.

Sprunt¹² treated 22 thyrotoxic patients with thiouracil in dosages up to 0.8 gm daily. Nine patients developed significant leukopenia, especially involving the granulocytes, with white-cell counts as low as 3000. The white-cell count regularly increased with cessation of therapy. When the drug was readministered in smaller doses, recurrence of neutropenia was infrequent.

In 1944, McGavack et al¹³ published a review of all toxic reactions to thiouracil that had been reported to that time and added their own experience with its use in 26 thyrotoxic patients. Three of these patients developed leukopenia, with intensification of the lymphocytosis already present. The respective white-cell counts were 3500, with 1400 neutrophils, 4500, with 1400 neutrophils, and 2500, with 1200 neutrophils. These neutropenic

reactions occurred between one week and five months following the daily administration of 0.3 to 0.4 gm of thiouracil. The drug was continued, with return of the hemogram to normal. No associated clinical symptoms of toxicity were mentioned. Two additional cases were reported by these authors, one with agranulocytosis and the other with neutropenia and both with clinical manifestations of toxicity. In the first case, agranulocytosis occurred in the sixth week of treatment at a thiouracil dosage level of 0.5 gm daily. Gingivitis, pharyngitis and fever were the chief clinical manifestations. On the forty-second day, the white-cell count was 3500, with no granulocytes. Stoppage of the drug and whole-blood transfusions were the only methods of treatment. After five days granulocytes appeared in the blood stream, and after thirteen days recovery was complete. Bone-marrow study revealed a decrease in the myeloid series and an increase in the lymphocytes, hematogones and reticulum cells. The authors ascribed this toxic reaction to the continued large dose of the drug (0.5 gm daily). The second case developed fever, urticaria and leukopenia after taking 0.5 gm daily of thiouracil for six days. Omission of the drug was followed by recovery over a ten-day period. Readministration of a single dose of the drug resulted in reappearance of all the toxic symptoms. During the initial toxic reaction, the white-cell count dropped from 12,200, with 10,120 neutrophils, to 9100, with 3640 neutrophils, at the height of the reaction.

Himsworth,¹⁴ in a discussion of the treatment of thyrotoxicosis with thiouracil, reports 1 fatal case of agranulocytosis in a series of 22 cases. The incidence of neutropenia in these cases is not mentioned.

A case of severe neutropenia following the administration of thiouracil for toxic goiter was reported by Meyer.¹⁵ Initially the patient received 0.6 gm daily for six weeks. Remission was incomplete, so that the dosage was increased to 1.2 gm daily for eight days. After this period, the drug was omitted for five days, when the same dose was readministered. Four days later, severe chills, a rise in temperature to 104°F and pharyngitis developed. The white-cell count dropped from its previously normal level to 2000, with 200 granulocytes. Treatment consisted of the omission of thiouracil and the administration of vitamin C, 40 cc of Pentnucleotide for one day, liver extract and sulfadiazine. Recovery occurred after ten days.

An additional fatality from agranulocytosis caused by treatment of the thyrotoxicosis with thiouracil has been reported by Kahn and Stock.¹⁶ This patient received 0.8 gm for two days, 0.6 gm for forty-two days and 0.4 gm for seven days, when pharyngitis, fever and agranulocytosis developed. Whole-blood transfusions, crude liver extract, Pentnucleotide, yellow bone-marrow extract

and penicillin were utilized therapeutically, without avail.

Rubinstein¹⁷ has recently reported a case of severe neutropenia following thiouracil treatment of carcinoma of the thyroid gland. Neutropenia developed after 0.8 gm had been administered for one hundred and eleven days, when the white-cell count was 1700, with 1000 granulocytes. The drug was then stopped. Five days later, the white-cell count was 750, with 75 granulocytes and 30 myelocytes. At the height of the neutropenic reaction there was no fever or ulcerative lesions in the mouth or throat, but transfusions were given. Recovery gradually occurred in the subsequent four weeks. Sternal-marrow studies were done on the seventh, eleventh, fifteenth and twenty-ninth days following the onset of neutropenia. Differential counts of the sternal marrow showed marked depression of the myeloid series, with an inverse increase in the erythroid series. In addition, there was arrest of maturation of the myeloid series, as evidenced by complete disappearance of segmented neutrophils, basophils and eosinophilic and basophilic myelocytes and markedly depressed numbers of nonsegmented neutrophils and neutrophilic myelocytes. These findings were taken as indicating that the agranulocytosis was caused by arrest of maturation associated with myeloid hypoplasia.

Rose and McConnell¹⁸ treated 37 thyrotoxic patients with thiouracil in doses up to 1.0 gm daily and observed 2 cases of severe neutropenia associated with pharyngitis and fever. In the first case, the white-cell count dropped to 1200, with 336 granulocytes, after twenty-three days of treatment. The drug was stopped and Pentnucleotide was administered. Two days later, the white-cell count was 1850, with only 222 granulocytes. Full recovery occurred after eight days. One week later, the administration of 0.2 gm of thiouracil daily for six days was followed by a drop in the white-cell count to 2400. The drug was again stopped. Beginning a month later, 0.2 gm of thiouracil was administered for a two-month period, without subsequent neutropenia. In the second case, pharyngitis and fever developed after nine days, associated with a white-cell count of 2200, of which 1520 were granulocytes. Stoppage of the drug was followed by recovery after three days. Resumption of thiouracil therapy was attempted after one month but was followed by fever, lymphadenopathy and pharyngitis after 0.4 gm had been administered. On this occasion the white-cell count remained normal, but the drug was omitted because of the other toxic symptoms. This patient had a previous history of allergy and iodine dermatosis. In addition to the severe reactions in this series, 14 patients with normal white-cell counts before thiouracil was given exhibited counts below 5000 within four to fifty-five days after institution of treatment.

sented in Table 4. The fasting blood sugar was 83 mg per 100 cc and the cholesterol 162 mg. The icterus index was 6. The basal metabolic rate before treatment varied between +19 and +29 per cent.

Thiouracil in daily doses of 1.0 gm was begun on November 9, and was continued at that level until November 12, when the dosage was reduced to 0.8 gm. This amount was ad-

TABLE 4 Hematologic Findings in Case 5

DATE	WHITE-GRANU- CELL LYCTE COUNT COUNT		DIFFERENTIAL HEMO- COUNT GLOBIN					RED- CELL COUNT	REMARKS
			N	L	M	E	%		
1944			%	%	%	%	%		
11-3	6,000	4,560	76	16	8		90	4.9	B M R +29%
11-10	6,000	3,660	61	25	10	4	94	5.5	B M R +17% on 2nd day of thiouracil, 1.0 gm daily
11-11	4,950	3,620	73	18	8				
11-12	6,400	4,550	71	21	6	2			Thiouracil re- duced to 0.8 gm daily
11-14	5,650	4,180	74	19	3	4			B M R +6%
11-15	5,100	3,820	75	17	4	4		3.9	
11-16 a m	4,000	2,320	58	32	2	7	84		B M R +1%
p m	5,100								
11-17 a m	4,100	3,080	75	20	2	3			
p m	4,400						84	4.5	
11-18	4,500	3,600	80	15	2	3			B M R -3%
11-19	3,950	2,840	72	18	7	3			
11-20	4,700	3,580	72	22	5	1			
11-21	5,500	3,850	70	22	3	5			
11-22	6,100	4,950	81	12	2	5			B M R. -6%
11-23	6,350	4,700	79	16	2	3			
11-24	4,900	3,820	78	18	1	3			
11-25	5,700	4,275	75	20	2	3			B M R. -6%
11-26	6,400								Thiouracil omitted
12-8	7,100	5,850	83	15	1	1	77	4.1	

ministered until November 26, when the patient was discharged. Thereafter, she took 10 drops of saturated solution potassium iodide daily. The response to thiouracil was prompt. At the end of 4 days of its administration, the basal metabolic rate had dropped to +6 per cent and there was marked clinical improvement. By the 10th day, it had dropped to -6 per cent, and it remained at that level until discharge. This remission has been further maintained by iodide medication.

Daily white-cell and differential counts were made during the administration of thiouracil to detect early toxic effects on the bone marrow. These are reported in Table 4.

Comment. This case is included to illustrate a benign hematologic reaction to the administration of thiouracil, characterized by slight leukopenia and neutropenia, with complete recovery in spite of continued administration of thiouracil.

DISCUSSION

In early animal investigations of the sulfur-containing compounds that simultaneously produce thyroid hyperplasia and inhibit hormone production, no reference is made to effects on hemopoiesis.⁶⁻⁸ When thiouracil and thiourea were utilized in the treatment of patients with toxic goiter, neutropenia and agranulocytosis appeared among the first toxic manifestations.¹⁻³ This effect was at first ascribed to overdosage or idiosyncrasy, but subsequent experience indicates that the etiologic mechanism of the hemopoietic depression is far from clear.

Astwood⁴ has reported 1 case of agranulocytosis and 1 case of marked leukopenia among 62 cases treated with thiouracil. The agranulocytosis in the first case was ascribed to the excessive dose of 2.0 gm daily. In the second case, which resembled Case 2, a patient with heart disease without thyrotoxicosis received 0.6 gm of thiouracil for sixty-two days and 0.3 gm for thirty-one days. On the

eighty-fifth day, sulfamerazine was given for a streptococcal infection of the finger, and by the ninetyeth day the granulocyte count had dropped to 100, with a white-cell count of 2000. Coincidentally, ulcerative stomatitis and pharyngitis developed. Recovery occurred after ten days. Despite the use of sulfamerazine, thiouracil seems implicated as the probable etiologic agent in this case because of the rarity of neutropenia during the first week of sulfonamide therapy. Although at first emphasizing the dosage factor in the causation of thiouracil neutropenia, Astwood has more recently raised the question of hypersensitivity tending to occur in allergic subjects.

Williams and Clute,⁵ in reviewing their experience with 72 cases of thyrotoxicosis treated with thiouracil, report 1 case of agranulocytosis and 1 case of neutropenia. In the latter case, the granulocyte count was 640 and the white-cell count 3200. Administration of thiouracil was continued, and the numbers of granulocytes and white cells returned to normal. These authors noted other mild leukopenic reactions, which they explained as part of the thyrotoxic syndrome, unrelated to the administration of thiouracil. In subsequent metabolic studies, Williams and his co-workers⁹ found the human bone marrow to be one of the tissues most highly saturated with the drug. They also found the concentration of thiouracil in white cells to be greater than that in red cells.

Gabrilove and Kert¹⁰ observed 1 case of neutropenia in 9 patients treated with thiouracil. The granulocyte count dropped from an initial level of 3420 to 1520 after 1 gm of thiouracil had been given for sixteen days, when the drug was stopped.

Paschkis and his co-workers¹¹ used thiouracil in the treatment of 17 cases of thyrotoxicosis and observed 1 case of leukopenia, with a white-cell count of 2500, after eight months of treatment with 1.0 gm of thiouracil daily. The count returned to normal within three days after stoppage of the drug, and was again depressed within forty-eight hours after resumption of treatment.

Sprunt¹² treated 22 thyrotoxic patients with thiouracil in dosages up to 0.8 gm daily. Nine patients developed significant leukopenia, especially involving the granulocytes, with white-cell counts as low as 3000. The white-cell count regularly increased with cessation of therapy. When the drug was readministered in smaller doses, recurrence of neutropenia was infrequent.

In 1944, McGavack et al.¹³ published a review of all toxic reactions to thiouracil that had been reported to that time and added their own experience with its use in 26 thyrotoxic patients. Three of these patients developed leukopenia, with intensification of the lymphocytosis already present. The respective white-cell counts were 3500, with 1400 neutrophils, 4500, with 1400 neutrophils, and 2500, with 1200 neutrophils. These neutropenic

and occasionally death. All patients in this group have been gravely ill but have had a recovery rate of 50 per cent.

The development of neutropenia and agranulocytosis following the administration of thiouracil is clearly not due to thyrotoxicosis, since these complications have occurred in patients without toxic goiter to whom the drug was administered as a metabolic depressant. Moreover, in many patients these deleterious reactions have occurred during remissions of the thyrotoxicosis induced by the drug.

Two other causative factors of the neutropenia have been postulated — namely, dosage and hypersensitivity. As regards dosage, one should consider both the size of the daily dose and the duration of administration. Thiouracil is not a cumulative drug, since its excretion is extremely rapid.⁹ Nonetheless, a depressing effect on the bone marrow may be cumulative with long-continued though small daily doses, as exemplified by Case 1, in which fatal agranulocytosis occurred after the patient had received daily doses of 0.2 gm of thiouracil for four weeks. Severe or fatal reactions have occurred at dosage levels ranging from 0.2 to 2.0 gm daily after six days to eight months. In many cases the dosage was appropriately reduced as the thyrotoxicosis abated, without preventing the onset of severe neutropenic reactions. The evidence is adequate that the dosage-time factor is not a controlling influence in the etiology of thiouracil neutropenia and agranulocytosis.

The factor of hypersensitivity in the production of neutropenic reactions has long been considered significant.²¹ Thiouracil definitely falls into the group of drugs that produce typical allergic manifestations — namely, drug fever, urticarial and other types of skin eruptions and reproductions of toxic symptoms with readministration in small doses. Chemically, thiouracil is closely related to barbituric acid, a compound whose derivatives have occasionally though rarely been reported to cause agranulocytosis.²²⁻²³ With this allergic background, the unpredictability of the toxic manifestations of thiouracil becomes clearer.

Whereas chemically thiouracil is nearest to the barbiturates, toxicologically it most closely resembles the sulfonamides. Many of the latter compounds similarly have antithyroidal effects like those of thiouracil but of lesser degree. This similarity is seen not only in the usual toxic reactions of drug fever, neutropenia and dermatitis but also in two more unusual ones — first, the ability to recover from severe neutropenia despite continuation of the causative drug, and second, the capacity of becoming desensitized to the drug with the repeated administration of small doses. Nixon, Eckert and Holmes²⁴ found that in 3 patients with agranulocytosis or severe neutropenia following the use of sulfadiazine, continued administration

of this drug in large doses did not prevent complete recovery. Williams and Clute³ have reported a similar experience with a case of thiouracil neutropenia with a granulocyte count of 640. Recovery occurred in spite of the continued administration of the drug.

Desensitization to thiouracil has been noted by several authors. Sprunt,¹² for example, found that its readministration in small doses after a neutropenic reaction was not often followed by recurrence of the neutropenia. Similarly, Rose and McConnell¹⁸ were able to desensitize 2 patients so far as the bone marrow was concerned by readministration of thiouracil after marked neutropenic reactions. Readministration of the drug is followed by phenomena of sensitivity oftener than by desensitization, but further study on this point is needed. If there is a true analogy with the usual protein type of allergy, attempts at desensitization should be made at extremely low dosage levels.

Whether the depressed function of the bone marrow is due to allergy or to overdosage, the actual production of neutropenia either is the result of arrest of maturation at the promyelocyte stage or occurs through direct destruction of white cells beyond the promyelocyte state. Bone-marrow studies have been reported by Rubinstein¹⁷ and by Ferrer, Spain and Cathcart,²⁰ and in Case 1 of this series. The findings in all cases have been the same, except that in ours the bone marrow showed large numbers of disintegrating forms as possible evidence of a destructive effect of thiouracil. Moreover, a similar destruction of granulocytes may occur in the circulating blood, a process suggested by Lawrence²⁵ as a mechanism for the leukopenia.

PREVENTION AND TREATMENT

The foregoing review of our own and reported cases indicates clearly the difficulties that surround the continued safe administration of thiouracil. No general rule can be laid down that will guarantee freedom from serious hematologic reactions. Dosage, duration of treatment, constant or intermittent therapy, associated clinical phenomena and premonitory symptoms have not proved safe guides. Serious reactions have occurred at both high and low dosage levels, with short and with long treatment and with both constant and intermittent administration of the drug. Premonitory symptoms are rarely present, and one severe neutropenic response has occurred without associated fever or ulcerative pharyngitis.¹⁷ Experience with hematologic reactions caused by drugs indicates that uneventful administration of a drug in normal doses for various periods of time in no way precludes the appearance of sudden unexpected sensitivity of the bone marrow.²⁶

One must therefore balance the unpredictable nature of the toxic effects of thiouracil against the seriousness of alternative methods of treatment of thyrotoxicosis. The available alternates are pro-

In 6 of these patients, the count returned to normal in spite of the continued administration of thiouracil. Of the remaining 8 patients, 1 showed an initial transient leukopenia after ten days, with normal counts for seven months, while taking 10 gm of thiouracil daily. At the end of this period, the white-cell count dropped to 2800. Further details were not given.

Nussey¹⁹ treated 27 patients with toxic goiter with thiouracil in doses ranging from 0.5 to 0.6 gm daily for periods ranging from three weeks to twelve months. White-cell counts were taken in all cases at intervals of one to several months while the patients were under treatment. Seven patients exhibited some degree of neutropenia or leukopenia during treatment, and in 2 cases initially low white-cell counts persisted or were intensified as the metabolic rate approached normal. In 1 case, the leukopenia was associated with a skin rash due to the drug, but in the remaining 6 cases no clinical symptoms of toxicity were noted.

Ferrer²⁰ has reported an additional fatality from agranulocytosis following the administration of thiouracil to a man of seventy with a toxic nodular goiter. The patient received 0.8 gm daily for three days, 1.2 gm daily for ninety-one days, 0.9 gm daily for twenty-nine days and 0.6 gm daily for seven days. The initial white-cell count was 9500, with 5700 granulocytes. The count gradually dropped to 5150, with 3350 granulocytes, during the first five days of treatment. Thereafter the white-cell count ranged from 5100 to 7400. Toward the end of the fifth month of therapy, the count was 1250, with 462 granulocytes. For the next two days the patient felt well, but on the fourth day a fever of 105°F developed, and on the fifth day pharyngitis appeared. This progressed in severity, and the patient died on the seventh day. During this period, the white-cell count continued to decline and reached 450, with no granulocytes, on the day of death. Pentnucleotide and whole-blood transfusions were of no benefit. Penicillin was administered during the last twenty-four hours, without effect. Post-mortem examination showed nonulcerative pharyngitis, multiple substernal adenomas of the thyroid gland, generalized dilatation of the heart, hemorrhagic lobular pneumonia and hemoglobin nephrosis (probably due to transfusion reactions). The bone marrow showed moderate granulocytic hypoplasia, with decreased adult neutrophils.

This review of reported cases in which thiouracil has caused varying degrees of neutropenia indicates that there are three main groups of cases—first, those with transitory neutropenia, entirely asymptomatic and often confused with the mild neutropenia and corresponding lymphocytosis of toxic goiter; second, those with significant neutropenia, frequently associated with clinical symptoms, especially fever and pharyngitis, readily improving

on stoppage of the drug and occasionally despite its continuation, and third, those with true agranulocytosis, corresponding in detail to the usual clinical syndrome of agranulocytic angina and often fatal.

The incidence of the first group of neutropenic reactions in all reported series occasioned little comment because spontaneous recovery usually occurred. Although ascribed by some authors to thyrotoxicosis rather than to thiouracil, these reactions seem clearly due to the drug, for three reasons. First, administration of the drug in these cases frequently produced a granulocyte count that was lower than the pre-treatment level. Second, omission of the drug was regularly followed by a

TABLE 5 Occurrence of Reported Case of Neutropenia and Agranulocytosis

SOURCE	CLASSIFICATION OF CASES*			DURATION OF TREATMENT PRECEDING GROUP 2 AND GROUP 3 REACTIONS
	GROUP 1	GROUP 2	GROUP 3	
Astwood ⁴	?	1	1	90, 37
Williams and Clute ³	?	1	1	Several days, 42
Gabrilove and Kert ¹⁰	1			16
Paschalis et al. ¹¹		1		240
Sprunt ¹²	9†			
McGavack et al. ¹³	3	1	1	6, 42
Himsworth ¹⁴	?	1‡	1‡	Not given
Meyer ¹⁵		1		54
Kahn and Stock ¹⁶			1‡	51
Rubinstein ¹⁷			1	111
Rose and McConnell ¹⁸	14	2		9, 23
Nussey ¹⁹	6	1		Not given
Ferrer et al. ²⁰			1‡	150
This series	1	3	1‡	8, 21, 24, 29

*Group 1 = transitory, asymptomatic leukopenia not requiring treatment or stoppage of thiouracil. Group 2 = neutropenia with symptoms usually requiring stoppage of thiouracil. Group 3 = agranulocytic angina.

†Some of these cases probably belong in Group 2 but not enough data were available for classification.

‡Fatality.

return of the depressed white-cell count to normal. Third, the decreased granulocyte count often developed as the thyrotoxicosis receded. No bone-marrow studies in this group are yet available, but it is probable that a temporary depression of the myeloid elements in the bone marrow occurs. An example of the slight and passing nature of this reaction is illustrated in Table 4 (Case 5). In this patient with mild thyrotoxicosis, the administration of thiouracil resulted in leukopenia and neutropenia after one week of treatment. The drug was continued, and the white-cell count returned to pre-treatment levels within one week.

The group of asymptomatic and transitory neutropenias caused by thiouracil merge into the second or intermediate group of cases, which may also be transitory but have usually shown clinical symptoms. In these cases, the granulocytes have generally numbered less than 1000, the clinical manifestations have varied from mild to severe and have usually included some degree of fever, pharyngitis and lymphadenopathy. Recovery has invariably occurred, usually with omission of the drug but occasionally in spite of its continued administration.

Cases in the third group are characterized by complete agranulocytosis, severe clinical symptoms

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THE CLINICAL SIGNIFICANCE OF DATA ACCUMULATED IN THE MEDICAL CARE OF YOUNG WOMEN

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CLINICIANS have not shown great interest in the study of the so-called "normal." The physiologists have made useful contributions, but these have not, for the most part, reached the clinician in such a way that he is led to apply the knowledge thus acquired. A review of the literature since 1918 reveals less than forty references dealing with the subject of normal physical findings as related to clinical medicine. A few of these deserve listing.¹⁻⁶ The Selective Service findings reported and publicized by Rowntree⁷ have brought up many questions about supposedly normal and supposedly healthy men. Members of the Grant Study at Harvard University have made some contributions to the study of normality in recent years.⁸⁻¹¹ Ivy⁶ has recently made a most helpful report on this subject. In spite of these scattered reports, it is still true that medicine in all its branches is chiefly concerned with major departures from a supposed norm — gross pathology and lesions that lend themselves to dramatic curative measures. But the expansion of knowledge in bacteriology and its application to

public-health practice suggest that in the future the most valuable contributions of medicine will be along the lines of preventive measures. From this concept it seems a logical step to study carefully the normal with all possible variations, especially as they relate themselves to the clinician's problems. This study will lead to knowledge of the ideal base line from which preventive medical measures can be planned. And as variations in the normal are learned in detail, it may become possible to detect the exact point at which a given disease has its onset — knowledge that is badly needed for understanding and prevention.

If the foregoing is true, there is distinct help to be had from the day-by-day accumulation of data of a college health service. Here may be found the materials with which to make tables of variables in physical and physiologic findings in young men and women of this particular age group. It is recognized that these persons comprise a selected group who have doubtless received better food and better protection from disease and accident than has the general population, yet there may be found in such data a wealth of material from which to learn the

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longed iodine administration, irradiation and thyroidectomy. Iodine administration is adequate in only a small percentage of cases, and irradiation is slow and unpredictable. Surgery is effective and quick in controlling a large percentage of cases. Thiouracil compares favorably with surgery in speed and certainty of treatment, but the expected fatality rate from thyroidectomy ranges from 0.5 to 2.0 per cent, and thiouracil has not yet resulted in mortalities of this magnitude, although the incidence of toxic reactions from the drug²⁷ is far greater than that of deaths following surgical extirpation. Furthermore, surgical deaths are most frequently encountered in the severely toxic cases, whereas thiouracil may cause fatal reactions in mildly toxic cases.

The proper treatment of thyrotoxicosis with thiouracil offers an opportunity to avoid the mortality associated with thyroidectomy in severely toxic cases. Thiouracil is capable in most such cases of reducing the high metabolic rate to a normal level and thus permitting one-stage thyroidectomy without danger of thyrotoxic crisis. Thiouracil is similarly useful as the sole agent of treatment in cases with an inadequate response to iodine therapy in which surgery is not feasible because of the physical status of the patient, because adequate surgical facilities are not available or because the patient refuses operation. Finally, thiouracil has a possible use in the management of persistent or recurrent thyrotoxicosis when adequate thyroidectomy has been performed without complete control of the disease or when there is unsatisfactory remission with iodides. The routine use of thiouracil as a substitute for iodides in the preparation of patients for thyroidectomy requires more study.

Thiouracil is definitely contraindicated in the continued management of patients with large or nodular goiters. The drug eventually controls the thyrotoxicosis, although taking longer to do so than in cases with moderate-sized thyroid glands, but leaves the gland in such a vascular state that removal is rendered more difficult. Toxic nodular goiters should be surgically removed because of the growth hazards of the nodule, both through the production of neoplastic lesions and by pressure.

Whatever the final position of thiouracil in the treatment of toxic goiter, it is clear that there can be no admissible use of the drug without thorough supervision of the patient. No false reliance should be placed on either dosage or duration of therapy. Once treatment is begun, white-cell counts must be made at least three times weekly, with differential counts when the total count drops below 5000. The occurrence of pharyngitis and fever is an unsafe guide to the blood picture, since these may develop relatively late in the course of the disease, indeed, in one fatal case agranulocytosis preceded these symptoms by several days.

These proposed safeguards for the use of thiouracil are indispensable because no proved protective measures are as yet available. In animals, it has been established that a component of vitamin B complex is essential for the prevention of nutritional cytopenia.²⁸ This component has been variously called "folic acid," "vitamin M" and "vitamin B_c." It is abundantly present in yeast, fresh liver and certain crude liver extracts. These prevent but do not always cure nutritional cytopenia. Spicer and his co-workers²⁹ have shown that sulfonamide-induced neutropenia and agranulocytosis in rats can regularly be prevented by addition to the diet of liver extract or yeast or of crude folic acid preparations from these foods. Daft and Sebrell³⁰ have shown that preparations of crystalline folic acid correct this sulfonamide-induced neutropenia after it has been established.

A similar approach has recently been suggested for the prevention of the neutropenia usually induced by thiourea in rats.³¹ Liver or folic acid was found to be successful in preventing this state. The application of this knowledge to thiouracil neutropenia in man remains to be elaborated. In monkeys suffering from nutritional cytopenia, however, cure with these materials is not always satisfactory,²⁸ since the animals enter an irreversible phase if the deficiency is allowed to progress too far. Thiouracil agranulocytosis in man, with a mortality rate of 50 per cent, is characterized by many elements of this irreversibility, so that treatment should be applied early and vigorously. It should consist of early omission of thiouracil, early institution of penicillin therapy as soon as it is suspected that spontaneous remission will not occur with omission of the drug alone, the use of folic acid, if available, or large amounts of liver or yeast and other measures that may be useful in agranulocytosis, such as the giving of Pentnucleotide and transfusions.

SUMMARY AND CONCLUSIONS

Of 61 patients with thyrotoxicosis and 1 with heart disease treated with thiouracil, 3 developed moderate to severe neutropenia and 1 developed fatal agranulocytosis.

A review of all reported cases of neutropenia and agranulocytosis caused by the thiouracil is presented. Various causative mechanisms of the toxic effect of thiouracil on the bone marrow are discussed.

Hypersensitivity is considered more significant than the dosage-time factor.

Thiouracil depresses the bone marrow, causing arrest of maturation at the promyelocyte state and possibly destruction of cells beyond this stage.

The indications for thiouracil and safeguards for its usage are described.

The prevention and treatment of thiouracil neutropenia and agranulocytosis are discussed.

are not particularly helpful, as shown by Best and Taylor's¹⁹ statement that leukocytosis occurs during menstruation and by the failure of Wright²⁰ and Stitt²¹ to mention any change whatever in the white-cell count at such a time. Curtis²² says that shifts in white-cell counts should not be overemphasized because of the effect of exercise and digestion in causing physiologic variations. Ehrenfest,²³ writes, "Investigators disagree in regard to a characteristic leukocytosis in the premenstrual week." Menkin,²⁴ in his work on changes in white-cell counts in relation to tissue damage, suggests that there might well be a premenstrual rise in leukocytes if the Smiths²⁵ are correct about the toxicity of menstrual fluid.

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menstruation and present knowledge of the mechanism utilized by the body in the distribution of white cells in response to physiologic changes. Neither of these reports speaks of menstruation and its physiologic effect on the white-cell count.

In Figure 2 is presented a graph of the total white-cell counts of normal women plotted against the day in the menstrual cycle on which the count was taken. One hundred and five of these counts were furnished through the courtesy of Dr. George Minot of the Thorndike Memorial Laboratory, Boston City Hospital, where they were done by Miss Elizabeth King and Miss Geneva Daland on healthy women who were technicians in the laboratory. One hundred and fifty-six of the counts were made on well college freshmen at the time of the routine physical examination on arrival at Radcliffe College. Com-

CORRELATION COEFFICIENT

$r = .01$ FOR DATA FROM DAY 13 PREMENSTRUALLY THRU DAY 11 POSTMENSTRUALLY

$r = -.06$ FOR ALL DATA

$r = .20$ FOR DATA COVERING 11 POSTMENSTRUAL DAYS

$r = -.26$ FOR ALL POSTMENSTRUAL DATA

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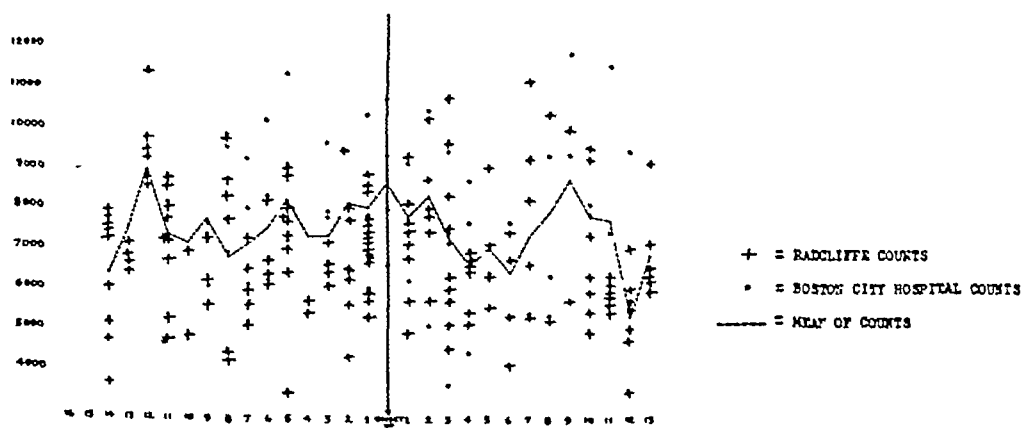


FIGURE 2 Variations in the White-Cell Counts in Menstruation

flow, after which there was a sharp drop. Havem²⁷ and Dirks²⁸ both believe that there is a definite increase in white cells during menstruation. Blumenthal²⁹ reports a decrease in white cells during menstruation. Novak³⁰ summarizes these reports in his monograph and concludes that there is no clear picture of what effect menstruation has on the white-cell count.

Two physiologists, Garrey and Bryan,³¹ made a careful report in 1935 that is extremely helpful in evaluating physiologic variations in white-cell counts due to age, posture, random activity, strenuous exercise, digestion, climate, pregnancy and emotional states. The report was brought up to date in 1943 by Sturgis and Bethell.³² Both these reports also deal with technical errors in such deter-

minate medical histories and careful physical examinations were done at the same time, so that counts of any student with detectable disease could be excluded.

Because of the slightness of the shifts in the counts it does not appear that exercise and digestion are significant. Furthermore, if the possibility of technical error is taken into account, this record of counts does not seem to show any distinct trend at any particular time in the menstrual cycle. The extremely low counts were repeated and remained approximately the same. The persons with counts under 4000 must be followed with a serious granulocytopenia in mind, such as that in the case reported by Jackson, Merrill and Duane.³³ The few counts above 10,000 may have various explanations worth

range of the probable ideal normal toward which to work to attain maximum health for the individual. Such knowledge may also prove useful in preventing diagnostic errors due to too narrow an interpretation of laboratory findings. One of the purposes of this paper is to point out the wide ranges of physiologic variation that are possible among normal young women. The information given below is intended to illustrate these ideas and to suggest the clinical use of this knowledge. The material is drawn from observations made in the routine work of the Department of Health Education of Radcliffe College from 1941 to 1944.

BLOOD-PRESSURE READINGS

We have been impressed with the number of young college women who have been told by physicians that they are suffering from low blood pressure. Such women have usually presented themselves to the physician complaining of fatigue. Our study of such complaints has convinced us that the causative factors associated with fatigue are usually lack of sufficient rest and exercise, stress of the emotional struggle that often accompanies the change from adolescence to adulthood, and the strain, real or imagined, of academic life. Seldom, if ever, is it found that a low blood-pressure reading and fatigue are directly related. Occasionally, following a severe infection or in the presence of a marked iron deficiency, such a reading is temporarily recorded. In most cases, however, the complaint of fatigue disappears when the factors outlined above are properly handled, yet the blood pressure remains low.

There is not much material in the literature that bears directly on this subject. Fisher and others¹²⁻¹⁴ published careful tabulations of insurance-company figures. Alvarez¹⁵ objected to such statistics because they represent only accepted applicants for life insurance. He¹⁶ was at one time deeply interested in collecting blood-pressure readings taken on young men and women at the University of California. He found that the women's readings were more uniform than the men's and averaged 11 mm. lower. In 1923, Symonds¹⁷ presented a huge number of blood-pressure readings of women of all ages that had been collected by life insurance companies. His figures are higher for the same age group than those of Alvarez and higher than those presented here. The objection raised by Alvarez is of course applicable. The more recent article of Robinson,¹⁸ in which he thoroughly reviewed the literature and discussed the whole question of hypotension is of significance.

The blood-pressure readings in 1000 college women between the ages of sixteen and twenty-two were recorded, and the findings are presented in graphic form (Fig. 1), as suggested by Alvarez.¹⁵ This graph shows the distribution of the systolic and diastolic readings in millimeters of mercury, taken with the armband sphygmomanometer with

the student in the sitting posture. All these young women had had a complete medical history and a careful physical examination, including hemoglobin determination, urinalysis and x-ray examination of the chest. In none was anything outside the

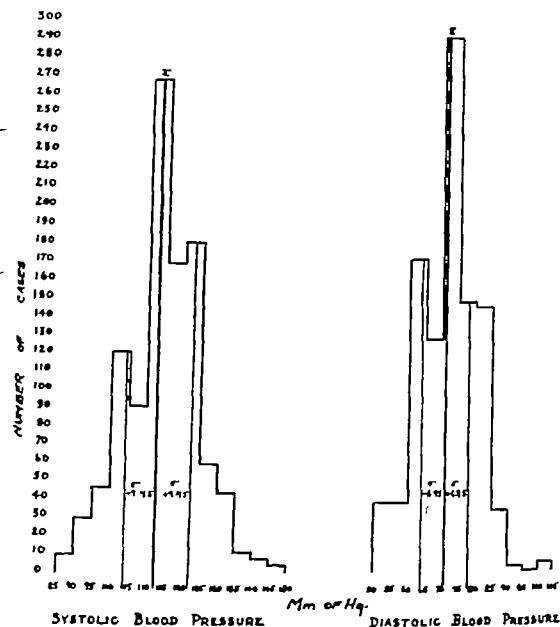


FIGURE 1 Blood-Pressure Readings in 1000 Young Women.

accepted range of normal detected. No student complained of faintness, dizziness or syncope at the time the blood-pressure reading was recorded, nor could such a history be elicited.

As the graph shows, the systolic pressure averaged 113, and the diastolic 71. It is of interest that there were seventy-eight systolic readings of 100 and under, and seventy diastolic readings of 60 and under, without any subjective symptom or clinical sign of so-called "hypotension." This record leads us to agree with Robinson¹⁸ that there is probably no such clinical entity.

WHITE-CELL COUNTS IN THE MENSTRUAL CYCLE

Not infrequently the physician in college medical practice is called on to decide how to handle the complaint of pain in the right lower quadrant of the abdomen in a young woman who is menstruating. This problem is almost always a complicated one regarding diagnosis and treatment. In our experience, the management of such cases is made more difficult by an elevated white-cell count, which might easily be attributed to menstruation. The finding of a normal-appearing appendix at operation on such a subject has raised the question what one may reasonably expect as physiologic variation due to menstruation. Hence, an attempt was made to ascertain the range of the white-cell count during the menstrual cycle.

Authors writing on this topic have come to a variety of conclusions. The standard textbooks

are not particularly helpful, as shown by Best and Taylor's¹⁹ statement that leukocytosis occurs during menstruation and by the failure of Wright²⁰ and Stitt²¹ to mention any change whatever in the white-cell count at such a time. Curtis²² says that shifts in white-cell counts should not be overemphasized because of the effect of exercise and digestion in causing physiologic variations. Ehrenfest,²³ writes, "Investigators disagree in regard to a characteristic leukocytosis in the premenstrual week." Menkin,²⁴ in his work on changes in white-cell counts in relation to tissue damage, suggests that there might well be a premenstrual rise in leukocytes if the Smiths²⁵ are correct about the toxicity of menstrual fluid.

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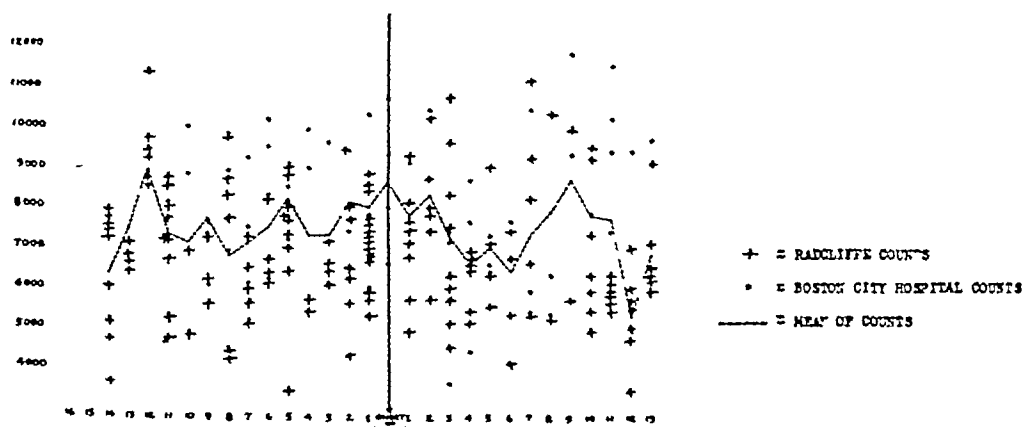


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minate medical histories and careful physical examinations were done at the same time, so that counts of any student with detectable disease could be excluded.

Because of the slightness of the shifts in the counts it does not appear that exercise and digestion are significant. Furthermore, if the possibility of technical error is taken into account, this record of counts does not seem to show any distinct trend at any particular time in the menstrual cycle. The extremely low counts were repeated and remained approximately the same. The persons with counts under 4000 must be followed with a serious granulocytopenia in mind, such as that in the case reported by Jackson, Merrill and Duane.³³ The few counts above 10,000 may have various explanations worth

bearing in mind for aid in the diagnosis of a surgical abdomen. After errors in technic are eliminated, one must consider the physiologic variations due to pain, as pointed out by Wolff³⁴ in a study of women in labor. Not enough cases have yet been studied to warrant conclusions, but experience in the Radcliffe Medical Office has been that the pain of dysmenorrhea does not ordinarily produce leukocytosis. An occasional case, however, is seen such as that of a nineteen-year-old student with a normal menstrual history except for slight dysmenorrhea on the first day of flow who reported to the office because of pain in the right lower quadrant of the abdomen on the third day of menstrual flow. When the white-cell count was found to be 19,000, the student was referred to a surgeon, who had her hospitalized. The surgeon kept her under observation for thirty-six hours, during which time the count fluctuated between 19,000 and 23,000. At the end of this period a laparotomy was performed. It revealed a normal appendix and no pelvic disease, such as endometriosis, to account for the leukocytosis. After operation the white-cell count returned to a normal level, and during a normal menstrual flow three months later repeated determinations showed counts between 8000 and 9000.

The explanation of a leukocytosis such as observed in this case is by no means clear. Possibly the emotional state of the student arising from fear of operation or anxiety about expense and loss of time from college work may be responsible. Work on animals^{35, 36} suggests this possibility, and some investigators³⁷ believe that affective states operate in human beings, a theory also proposed by Garrey and Bryan.³¹

The present method of study is admittedly crude, and careful differential counts, such as the Schilling and Arneth counts, might, if done over long periods of time on normal menstruating women, bring out changes related to menstruation. Smith believes that a rise in leukocytes occurs twelve to twenty-four hours before the flow begins.³⁸ The material presented here should be followed by larger numbers of similarly taken white-cell counts before the final word is said on the physiologic variation in counts during menstruation. For the practical purpose of differential diagnosis, however, there is seen in this study no suggestion that the white-cell count undergoes a physiologic shift at any time in the menstrual cycle. The clinician and the surgeon must continue to make the diagnosis of a surgical abdomen on the basis of the history and physical findings. It seems a fair conclusion that, barring an occasional subject whose excessive response to a "crisis" produces a leukocytosis, an increase in white cells beyond 10,000 per cubic millimeter in a menstruating woman has to be explained

obtain a red-cell count and a hemoglobin determination. Often these values are below the textbook norms: the hemoglobin reading is about 70 per cent on the Sahli scale, and the red-cell count is below 4,500,000. The physician then prescribes iron by mouth, and expects that the sensation of fatigue will yield to the establishment of a high hemoglobin level.

Our experience with young college women who complain of fatigue and who present the laboratory findings described above has not been consistent with this expectation. First, a rise in the hemoglobin level to what is considered normal does not by any means always relieve the fatigue. Second, there are many cases in which proper therapy as outlined by Castle³⁹ does not result in a change in hemoglobin level. Care has been taken, of course, in the treatment of these cases to be sure that there is no source of chronic blood loss, digestive disturbance or chronic infection that might be relevant. Although we have been unable to diagnose them as such, in this group there are doubtless cases of deficiencies of necessary substances other than iron—a consideration that Heath⁴⁰ discusses.

In contrast to those who complain of fatigue, there is another group, that of students who do not complain of fatigue and who appear to be in good health, yet who show, in the course of routine physical examination, low hemoglobin levels of which they were unaware.

In an attempt to discover some of the reasons for these findings, a careful study was made of 12 students during the six months between November, 1942, and May, 1943. This period was selected because of the prevalence of infections in New England at this season and the possible bearing that they might have on the problem. The students were not among those who had complained of fatigue or who had shown any symptoms of ill health, but were selected at random from the number who responded to an appeal for volunteers. All of them were carrying a full college course. Ten of them also carried a fairly heavy load of student, social and war activities.

A detailed history of each student was taken in the attempt to discover any possible source of iron deficiency prior to this study. The students were given a set of questions, to be answered by their mothers, relative to the presence of anemia in the mother during pregnancy, serious childhood infections or childhood feeding problems that might be relevant. A full record was made of adolescent medical histories for information concerning errors in diet, menstrual disturbance or any chronic diarrhea, infection or blood loss, however slight. A thorough routine physical examination, such as is given to all entering college students, was included. A gastric analysis was not done, although one would be desirable, since, as many authors have pointed out,⁴¹⁻⁴³ proper iron absorption depends on the acidity of the gastric contents.

ANEMIA AND FATIGUE

When a young woman complains of fatigue, one of the first steps in diagnosis and treatment is to

During the period of the study each volunteer reported every two weeks to have a sample of blood taken from a vein. A Sahli hemoglobinometer was used*. The same tube was employed for each reading. At each of these visits a brief history was taken, with special reference to the complaint of fatigue, diet irregularities, any unusual stress and strain that resulted in insufficient rest, physical exercise, menstrual irregularities and intestinal upsets. From each sample of blood a red-cell count and a hemoglobin determination by the Sahli method were made. The findings were plotted on a graph against the dates of the students' visits (Fig 3). From these

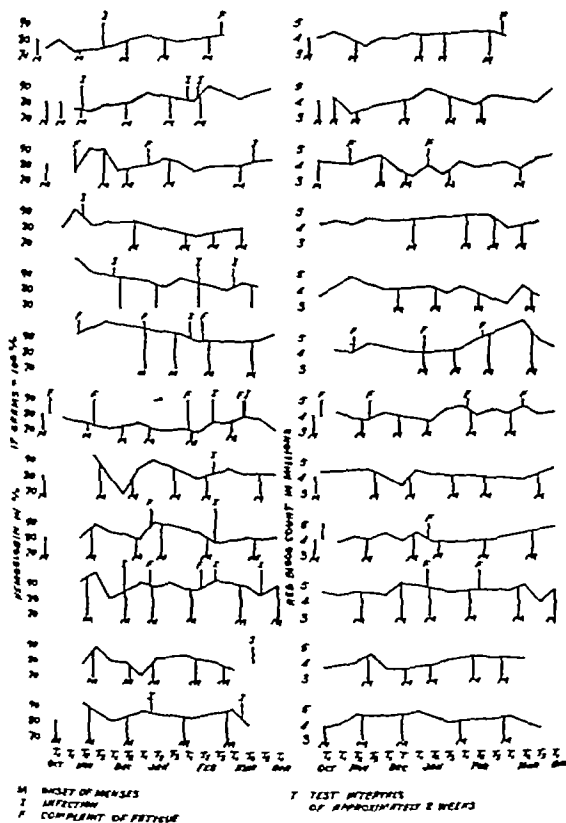


FIGURE 3 Variations in the Hemoglobin Levels and the Red-Cell Counts in 12 Young Women.

graphs an attempt was made to find variations that might be correlated with any of the facts elicited from the histories — especially, of course, the complaint of fatigue.

The case histories furnished what must be a fairly usual assortment of stories. Among the parents of the 12 volunteers, two mothers and one father gave a history of anemia. Two of the students had been feeding problems, and 3 had had a serious infection in early childhood, — 2 cases of scarlet fever and 1 of pneumonia. The adolescent histories up to the date of the study included 4 cases of poor eating habits, — that is, no breakfast, many sandwiches and soft drinks and too little meat and milk, — 7 of three or more moderately severe head colds

each winter, 1 of chronic gastric upsets and 4 of intermittent bouts of diarrhea not considered serious enough to require medical attention. The single menstrual disturbance was an irregularity that did not result in excessive blood loss. One student in 1941 had had a basal metabolic rate of —17 per cent, which, after thyroid therapy, returned to within normal limits. Four students gave a history of easy fatigability prior to the period of this study, and 7 complained of fatigue at different times during this period. These complaints, however, were not spontaneous but were elicited only by questioning.

The striking fact is that, although at some time or another during the study seven of the graph curves showed hemoglobin values of 70 or 80 per cent, these occurrences did not coincide with the times at which the complaint of fatigue was present. Making allowance for experimental error, there are still no significant variations in the curves described by the records of these levels, and no relation between a red-cell count and hemoglobin slightly below normal and fatigue, menstruation or infection. Infections during this period of study were few and not severe, consisting of 1 case of German measles, 1 of mild otitis media and the usual run of upper respiratory disease and what is loosely termed "grippe." Menstruation has already been shown by workers in this field to produce no definite variation in the red-cell count and hemoglobin values provided that other factors, such as dietary deficiency and infection, are absent.^{26 44 45} This fact is emphasized in the graphs presented here.

In an analysis previously made by me of the diet of the average college student, diet histories covering four complete days for each student were taken in minute detail from thirty students. The North End Diet Kitchen of the Massachusetts General Hospital found that every one of these diets was deficient in iron and that all but two were deficient in thiamine chloride, according to present standards. It is reasonable to infer from this, therefore, that the diets of the 12 students in the group under discussion — 4 of whom gave frank histories of inadequate and poorly planned nutrition — may have shared these deficiencies. In view of Heath and Patek's careful analysis⁴⁰ of present evidence of the amount of iron the body needs daily to maintain its optimum level, the dietary lack of iron in young college women is probably not highly important. It is possible, however, that this is a factor in the otherwise inexplicable low hemoglobin levels in some students who have no clinical complaints, since there is a greater demand for iron in young women because of menstrual blood loss.

From this study it is concluded that since red-cell counts and hemoglobin levels slightly lower than normal are apparently not related to fatigue, menstruation or infection and produce no other symptoms, the body is able to manage efficiently with what has been considered to be less than the normal blood level. It may be wise, however, to treat this

*Sahli standards were calibrated so that a hemoglobin of 100 per cent was 100 mm per 100 cc. of blood.

condition to prevent an iron deficiency at a later date when, as Heath¹⁶ suggests, the body demands more available iron—as in pregnancy. Iron-deficiency anemias due to blood loss or to severe infection do, of course, produce a complaint of fatigue that responds dramatically to the proper use of iron by mouth. There is, nevertheless, much that is apparently still unknown about the human body's need for and use of iron. This study indicates the need for further research in the great problem of fatigue.

* * *

These three short studies are presented to emphasize the value of analysis of normal findings and their variations. Such knowledge will be helpful, as Alvarez¹⁵ points out, "to spare patients pain and needless treatment" and will add to the general understanding of so-called "normal." Although the findings presented here do not corroborate widely held opinions regarding the significance of certain levels of blood pressure and hematologic values, it is through the pursuit of such inquiries as this that preventive medical measures and methods of detecting the onset of disease may eventually be learned.

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MEDICAL PROGRESS

MENSTRUATION, ITS DISORDERS AND THEIR TREATMENT*

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CONSIDERATION of menstruation is organized as follows factors in normal menstruation character of normal menstruation, disorder in frequency of flow, disorder in duration or amount of flow, disorder in frequency, duration and amount of flow and treatment

FACTORS IN NORMAL MENSTRUATION

To produce the physiologic shedding of the mucosa at the conclusion of a sterile cycle, two separate endometrial processes are closely integrated. One is the cytologic development of this tissue from a proliferating to a secretory or functional membrane, which then gradually changes to a predecidua. The second endometrial process, distinct from the first, although usually associated with it, is the establishment of the bleeding potential, the activation of which causes the destruction of the superficial portion of the predecidua.

The Predecidua

The cellular changes marking the sequences in mucosal development during the menstrual cycle have been frequently described since Hirschmann and Adler's¹ time (O'Leary,² Bartelmez³ and Rock.⁴) Growth of what is left after decidualization of the upper layers proceeds to full proliferation of the tissue. After ovulation, this quickly changes into the functional endometrium. Finally, during the last premenstrual week, this is transformed into the thick compact layer of the predecidua. Proliferation is known to be the effect of estrogen from the growing follicles. Secretion is the result of the addition of gradually increasing amounts of progesterone from the young corpus luteum. The predecidua is the result of the prolonged action of progesterone and estrogen and represents the limited extent to which the imperfect corpus luteum of futile ovulation can transform the lining of the uterus into the decidua of pregnancy, the full blossoming of the endometrium.

The Bleeding Potential

What is the nature of this obscurely termed "bleeding potential"? It is a "quality" not a "thing." As yet it is known only in action, not in being. Considering Markee's⁵ observations and the Smiths's⁶ biochemical findings, it seems best de-

scribed as the susceptibility of highly differentiated arterioles to products of endometrial catabolism. This ability to bleed on the part of the uterine mucosa frequently is normally established in the primate endometrium without the cytologic changes that produce the particular function of the tissue. That is because the potentiality to bleed is initiated in the endometrium by the estrogens only. To be sure, the follicular hormone, as well as its two commonest derivatives, also stimulates proliferation of the endometrium, and usually these two functions of estrogen — growth of endometrium and development of bleeding potential — are ambivalent, but often they are not. So, even in the absence of pathology, bleeding sometimes occurs from a hypoplastic mucosa. The bleeding potential, although induced solely by the estrogens, is enhanced not only by continued action of an estrogen but to a greater extent by action of succeeding progesterone, especially if this is accompanied by an estrogen. The combined influence of the two hormones establishes the ability to bleed as a normal property of the predecidua. It must be remembered, however, that progesterone is not essential to the process of flow and that this frequently is evolved in the non-secretory, merely proliferative, endometrium.

In those subprimate mammals in which, as in human beings, the corpus luteum is formed whether or not the egg is fertilized, the endometrium proceeds, as in women, from proliferation to formation of the predecidua, but the useless secretory tissue is partly shed and doubtless partly reabsorbed without the loss of blood. That this endometrial growth to a predecidua can take place in human beings without the second process — the synchronous development of the bleeding potential — is an unlikely possibility. Hence, in man disappearance of the predecidua without activation of the bleeding potential is not to be expected. Among several thousand patients in whom biopsies of the endometrium were studied, I have seen only one case in which a full secretory endometrium was changed to a subsequently proliferating tissue without a recognizable intercurrent bloody flow. As the patient had long been amenorrheic and was being treated for the condition, it is hard to believe that appreciable menstruation was either unobserved or denied. Occasionally there is found a pregnancy that starts after several months of amenorrhea and is thus of shorter duration than the absence of flow.

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Failing fertilization, would such a case be one of occult ovulation and corpus-luteum formation, or would flow have terminated the amenorrhea two weeks after rupture of the follicle? I do not know. One should be mindful, however, of extreme hypomenorrhea, that is, cyclic catamenia of only a few hours' duration, which is discussed later. This differs by only a few cubic centimeters of blood from complete failure of the bleeding potential to develop while the endometrium grows.

Activation of the bleeding potential is dependent on a critical change in the absolute or the proportional amounts of the various estrogens. Such critical change may occur with prolonged absorption by the blood of the estrogens from active growing follicles or from injected or ingested material. It is also found when a sufficiently high concentration of estrogenic substances in the blood is reduced after cessation of further increments from follicles or from medication. The critical change is also made when progesterone that has quickly followed or has been active concurrently with an estrogen is withdrawn. This last condition is typified by normal menstruation. Clinical evidence is mounting that activation of the bleeding potential also occurs when prostigmin evokes hyperemia of the endometrium. Does this drug merely lower the threshold of susceptibility of the local vascular system to the mysterious agent, a product of the catabolism of the endometrium⁶ which starts the bloody destruction of the mucosa? Markee⁷ has given an enduring classic description of how the bleeding starts in the monkey. There is every reason to believe that the process in human beings is quite similar. Markee states

Menstruation was studied microscopically in intraocular endometrial transplants in over three hundred cycles. The following sequence of events occurs in both ovulatory and anovulatory cycles, following castration, after injections of oestrin and after spinal transection. The superficial two thirds of the transplant, supplied by coiled arteries, becomes completely anemic. Four to twenty-four hours later circulation temporarily resumes in single arterial fields (the remainder of the transplant remaining anemic) and almost immediately blood escapes either from a capillary or from an arteriole. It usually escapes from only one point and a hematoma may form. Occasionally it oozes for a short distance along one of these vessels, in which case a hematoma forms more slowly. Hematomata resulting from rupture of a vessel form and begin to discharge in one to twenty-five minutes, while those formed by diapedesis may persist for thirty-six hours. There is an occasional reflux of blood from a vein whose capillary bed is either constricted or destroyed. Single hemorrhages last from six seconds to twenty minutes. They are arrested by contraction of the appropriate coiled artery or its branch. Blood from these primary hemorrhages seldom clots. Fright at this stage causes, within fifteen to twenty-five seconds, reopening of the arteriole, which for five to fifteen seconds delivers blood that promptly clots. In many cycles, congestion and nearly complete stasis precede the anemic stage by 2 to 4 days.

Nonhormonal Factors in Bleeding

Although endometrial bleeding in the absence of local pathology may be dependent for its occurrence on the ovarian hormones, it is surely prolonged or increased by other than hormonologic agents. Among

possibly modifying factors, one should note particularly the clotting qualities of the blood and the nature, especially the rapidity, of the tissue-repair processes. On these doubtlessly depends the permanent closure of the spiral arterioles, which are laid open to the uterine cavity when denudation occurs, although, as Markee⁷ has noted, cessation of bleeding is first accomplished by recontraction of the vessel. Venous congestion, as well as inflammatory hyperemia, increases the flow. Contraction of the interlacing uterine muscle bundles probably helps to stop the loss of blood from the exposed and broken vessels by constricting the uterine arteries. Elements of diet or hygiene that may affect any of these processes should be included, although in a subordinate position, among the factors giving expression to the bleeding potential.

CHARACTER OF NORMAL MENSTRUATION

Many forms of catamenia, because they are found in healthy women, must be considered normal, although they differ widely from what may be called the pattern of perfect menstruation. Ideally the flow would occur only two weeks after ovulation, and ovulation would start only and always at puberty, at about the age of thirteen, and after puberty it would unfailingly occur periodically, except during pregnancy and lactation, and it would abruptly cease at a definite age, perhaps in the forty-fifth year. Ideally, too, the menstrual flow would be painless, persist for a reasonable stated period and be moderate in amount. Unfortunately such a complex mechanism, involving so many factors, functions thus ideally for not more than a few months at a time, and then in only comparatively few women.

Puberty is a phase, not a moment, in sexual development. It is during, not at, puberty that flow ordinarily starts. It may appear early or late in the period of sexual maturation. Puberty is the season during which the process of follicular development that has been in operation in the ovaries since before birth reaches fulfillment of function, ovulation. Although follicles in varying numbers approach the rupture stage, only an occasional one at irregular intervals is at first likely to complete the process. Thus there are, aperiodically, sufficient amounts of estrogen either to evoke full proliferation of the endometrium or to develop therein the bleeding potential. As has been said, this may be activated and bleeding ensue at equally irregular intervals by the critical breakdown of this estrogen alone, such as always occurs in the presence of progesterone but may take place without it. If the supply of estrogen is small, bleeding may be absent for many months. Then again, ovulation, and hence menstruation, may be rhythmic almost from the beginning. It may be said that, normally, puberty has been achieved when the process of ovulation has

been established, in that eggs ripen and are released at intervals characteristic of the human species. Furthermore and for obvious reasons, the term "normal menstruation" should be limited to that which follows ovulation.

Periodicity of Menses

Growth of follicles, which produce estrogen, evokes the bleeding potential, "withdrawal of hormonal support, with its accompanying change in endometrial metabolism and 'toxin' formation,"⁸ precipitates the bleeding itself, but only the corpus luteum gives the bleeding true periodicity. This is so because the human corpus luteum functions for about two weeks. During these two weeks its specific secretion, progesterone, while enhancing the bleeding potential already inaugurated by estrogen, also inhibits its expression, probably by its influence on estrogen metabolism. Part of this time, increasing concentrations of estrogen in the blood have been augmenting the suppressed menstrual urge. With the decadence of the corpus luteum toward the end of the fortnight, the supply of follicular estrogen and of progesterone diminishes, inhibition is removed, and the bleeding potential is activated.

The corpus luteum, probably by means of progesterone, is also responsible for the regression that is common to all intact partly ripened follicles. When its dominance ends after the two weeks of its function, many other nonatretic follicles start to mature. Ordinarily, during the menarche, after about two weeks, one of them ripens, ruptures and forms another luteal gland. Thus is periodicity given to recurrent flow by the corpus luteum.

In the absence of ovulation, so far as is known, the corpus luteum does not form. The fortnightly inhibition of the bleeding potential is absent, as well as the repression of follicular growth. Follicles grow and regress irregularly, estrogen is produced, at times in large quantities, at times in small. The bleeding potential is developed and activated in the presence of an abnormally high estrogenic titer or of sudden decreases in the amount present, but without reference to time. Thus there is aperiodicity in the recurrent flow because of the absence of the corpus luteum.

Length of normal cycle. First, what may be considered neither too many nor too few periods? Somewhat misleading are our three terms for normal uterine discharge — menses, menstruation and catamenia, indicating, by derivation, "monthly flow." Never for long do cycles conform to the unnatural but civilly essential calendar month. With the lunar month of almost 29.5 days they are in much closer accord; but in no woman are the menstrual cycles of constant length however frequently they

may approach this rhythm of the moon. In applying definitions to this subject of normal cycle-lengths, any essayist must claim sanctuary in "the purposes of discussion," and reasonable limits must be allowed to his refuge.

The cycle in human beings is customarily considered to be about 28 days long, with flow starting on each twenty-ninth day. The inaccuracy of this concept has already been shown (Fluhman⁹ and Haman¹⁰). Our analysis of six consecutive cycles recorded by each of a sample group of 100 young fertile women, all wanting to know their ovulation time for contraceptive purposes, is confirmatory. Most normal cycles are within the range of 28 ± 4 days, that is, normal menstruation usually starts not earlier than the twenty-fifth day nor later than the thirty-third day of a given cycle. Excursions beyond these limits among our group of 100 normal women, however, were not infrequent. Twenty-one patients, during the recorded six cycles, jumped the range, once, 18, twice, and 12, three or more times. Of the six hundred cycles, there were ninety-nine (16.5 per cent) beyond the range of 24 to 32 days. I believe it is fair to consider that menstruation is, to some extent, disordered if it habitually occurs oftener than the twenty-fifth day or less frequently than the thirty-third day. As previously stated, the typical normal cycle may be considered as 28 ± 4 days.

Most women who ovulate regularly will be found during six consecutive months to menstruate within this wide range and often within narrower limits. If \bar{x} be taken to mean any one figure within the span of 28 ± 2 days, then $\bar{x} \pm 2$ days, which at most will be 28 ± 4 days, limits the range of 38 of our 100 sample patients. Eleven more had only one cycle greater or less than this, 13 had two, 2 had three, and the other 36 were moderately irregular, although they sometimes menstruated within the limits of 28 ± 4 days.

Amount and Quality of Bleeding

When the nonhormonal factors of clotting, tissue-repair, muscle tone and blood supply are normal, the amount and duration of bleeding and the quality of the discharge are roughly proportional to the degree of proliferation and to the area of tissue destruction. Of influence also is the length of time during which the bleeding potential is activated. Throughout the two weeks of luteal function, progesterone stimulates a fairly uniform development of the predecidua over most of the fundal cavity, and does it to the same extent during progressive cycles, so that the amount of tissue developed and the area covered are repeatedly essentially the same. Furthermore, when the bleeding potential in this tissue is activated on the withdrawal of estrogen and progesterone, the bleeding mechanism is started

over the whole area, usually within forty-eight hours. Promptly thereafter, recontraction of the arterioles, clotting and repair processes function, and in due time the bleeding ceases. Thus in cycle after cycle the amount and the duration of the flow are similar.

When ovulation fails, and there is no luteal hormone, estrogen from an indefinite and ever-changing number of well developed follicles establishes a bleeding potential of equally variable intensity in an endometrium that has proliferated in different degrees. According to the Smiths,⁸ "Bleeding when it does occur due to temporary drops in estrogenic support to the endometrium, fails to be accompanied by 'the trigger' mechanism of both hormonal and endometrial origin that makes for normal follicle maturation and periodicity." Furthermore, activation in the solely proliferative endometrium, unlike that in the secretory tissue, is not fairly synchronous over the whole area, often occurring in patch after patch during many days or weeks. Thus in successive periods of flow are the amount and the duration of the bleeding and the quality of the discharge variable in the absence of ovulation.

Again for purposes of discussion, one must be somewhat arbitrary in defining the limits of the flow of normal menstruation. It varies in amount from day to day and in the number of days during which it persists. In general, it lasts for not more than seven days and not less than three, and requires an average of four napkins a day. A discharge that stops sooner or is less profuse than these limits, constitutes hypomenorrhea. Mild degrees of this seem to me to be more frequent than hypermenorrhea, which exceeds either of these limits.

DISORDER IN FREQUENCY OF FLOW

The dominant qualities of flow may be listed as periodicity, frequency, duration and amount. Since the incidence, the length and the quantity of flow may vary from what may be considered typical of normal decidualization, there appear various forms of menstruation, not all of which should be considered harmful. One distinguishing characteristic of normality is almost always present. This is periodicity (measurability or regularity) of the recurrent cycles. Except in cases of extreme oligomenorrhea, whenever flow occurs aperiodically (immeasurably or irregularly) one may be sure that ovulation is incomplete or more infrequent than are the phases of flow. Aperiodomenorrhea then is abnormal, for it bespeaks a failure of ovulation. Reference to what has been written above concerning the role of the luteal secretion, progesterone, both in temporary inhibition of follicular development and in the metabolism of estrogen, will explain the relation biopsy on the first days of irregularly recurring catamenia will prove it. As failure of ovulation is dysfunction, this type of flow, aperiodomenorrhea,

is dysfunctional. Further consideration of it is postponed.

Among the forms of functional, therefore periodic, flow are oligomenorrhea (few periods) and polymenorrhea (many periods), as well as hypomenorrhea (little flow) and hypermenorrhea (much flow). All these forms, with the occasional exception of marked oligomenorrhea, have a discernible periodicity. This is because the fortnightly luteal function of the ruptured follicle is more or less unimpaired. But luteinization also ensures two other qualities of a flow that is functional—duration and amount. Reconsideration of the parts played by estrogen and progesterone in the formation and integration of the predecidua and the bleeding potential and of how decidualization occurs will show why this is so.

Amenorrhea

This is but a comparative term, as applied to otherwise normal menarchial women, for failure to flow, usually is limited to months or years. Almost never is menstruation completely absent from puberty to the menopause. As against oligomenorrhea (few periods), what infrequency should be called amenorrhea? Customarily, it is that of four months or more, although flow may be absent for many years.

Except possibly in the very rarest of cases, mentioned above, in which there is absence only of the bleeding potential,—theoretically a sensitivity of the specialized arterioles to the catabolic products of the endometrium,—failure of menstruation reflects failure of ovulation. The hypophysis does not secrete proper amounts of follicle-stimulating or of luteinizing hormone, or the primary follicles, for some unknown reason, are insensitive to normal hormonal stimulation. When pituitary failure is not evidenced by dysfunction of the other endocrine glands, there is usually only partial lethargy of the follicles. In some cases it is surprising how nearly many of these approach normal size, giving estrogen titers of low normal values and thus stimulating a fair degree of endometrial proliferation, however, neither an egg matures, nor is the decrease in estrogen sufficient to cause destruction of the endometrium. Thus amenorrhea is essentially a gross dysfunction of ovulation.

Oligomenorrhea

When cycles are habitually longer than thirty-two days, the condition is termed oligomenorrhea (few periods). In 100 barren women, we found only 4 with this condition, among 100 fertile women, there were 7. If the phases of flow resemble each other in duration, quality and quantity of discharge, biopsy during the week before flow will almost certainly show that ovulation took place about fourteen days before the menses appeared. Women who menstruate at long intervals, but always similarly, ovulate at equally long intervals and thus function normally during approximately four weeks before

the onset of flow. Preceding these four weeks, there is disruption of the reciprocal activity of the pituitary gland and the ovary. When the interplay takes place, it performs in proper fashion. True oligomenorrhea is thus a disorder of ovulation rather than a dysfunction of menstruation.

Polymenorrhea

When a woman usually, not necessarily always, flows periodically (measurably or regularly) oftener than every twenty-fifth day, she may be said to have polymenorrhea. Of 100 reasonably fertile patients in our Rhythm Clinic, only 1 fell into this group, of 100 periodically menstruating barren women in our Fertility Clinic there were none.

Biopsy studies reveal several facts of great clinical significance among patients with polymenorrhea.

In the first place, there is a lower limit to the frequency of functional (postovulatory) flow at twenty-one days. Almost, perhaps all, women who flow consecutively as early as the twenty-first day following the onset of previous menstruation will be found to have only a proliferative endometrium, thus manifesting the nonovulatory or dysfunctional nature of the flow.

Secondly, probably more than half of those with polymenorrhea — that is, those whose cycle lengths lie between twenty-two and twenty-four days inclusive, — show in their endometrium, at the time of flow, a luteal influence of about fourteen days' duration. These therefore ovulate at the normal time in their cycles — about the fourteenth day of flow, although earlier than the fourteenth day of the cycle. The shortening of the cycle occurs in the preovulatory phase, when the follicles grow and an ovum matures. The postovulatory or luteal phase extends for about fourteen days, as is usual in patients of normal range.

Thirdly, some with such short cycles are discovered by biopsy to flow from an endometrium that shows less than a fourteen-day luteal influence. The endometrium at menstruation is secretory but not of the ripe predecidual type. These women then ovulate less than fourteen days before the onset of the succeeding flow, an important deviation for the purposes of contraception by periodic continence.

Finally, an occasional patient complains of menstruation as often as every two weeks, or that discharge reappears for a few days about a week after menstruation has ceased. Biopsy reveals that such patients flow alternately from a full secretory and from a late proliferative endometrium. Their real menstrual periods occur within usual time limits; the intermediate phases of flow occur about fourteen days before the period, at ovulation time, and are merely an exaggeration of the ovulatory bleeding that doubtless takes place in all other women to a less extent, at or just after ovulation. (Hartman¹¹ found

this in 75 per cent of his monkeys.) It is usually so slight as to pass unnoticed, often consisting of only enough to give the cervical mucus a transitory dark-brown tinge. In case the flow is noticeable, only alternate periods resemble each other. The condition, furthermore, is usually but transitory and intermittent.

DISORDER IN DURATION OR AMOUNT OF FLOW

Hypomenorrhea

Very occasionally the clinician sees a woman whose cyclic flow obtains for only a day or two, or one whose discharge requires only one or two napkins a day. The endometrium in these cases, although constituting a true predecidua, is usually not so thick as commonly found. The cytologic make-up, denoting the effect of estrogen and progesterone, is the same, but there is a paucity of tissue. It is possible that in some of these cases the qualities of the nonhormonal factors are reversed. Parenthetically, it may be said that this condition has not been found to cause infertility. The tiny trophoblast apparently finds, even on this thin mucosa, all that it needs for implantation, and its stimulating influence provides the necessary increase of tissue.

Hypermenorrhea

Prolonged or voluminous phases of flow, which resemble each other, whether at normal intervals or as in polymenorrhea or oligomenorrhea, will be found on biopsy to come from a true predecidual lining. In such cases, there is no cytologic evidence of deficient corpus-luteum secretion. Sometimes, just before the flow begins the endometrium is thicker than it is in most cases, but the constituents are the same.

Reference to the foregoing discussions of non-hormonal factors of flow makes it clear that retardation of clotting or of repair of the areas exposed by denudation, with their many torn capillaries or severed arterioles, as well as delay in the reconstruction of arterioles, may permit prolongation of hemorrhage although the hormones involved are in normal concentration and proportion. Similarly, a conceivable inordinate complexity of the vascular tree or an undue venous pressure may increase the number of bleeding vessels, or myometrial atonia may allow comparative hypertension in the terminal arterioles that are opened by disruption of tissue. But just as there is a disparity between bleeding potential and endometrial proliferation in some cases of dysfunctional flow from a hypotrophic mucosa, so, theoretically, in functional flow from a predecidua the hormones involved may set up exaggeration of bleeding while causing only the ordinary degree of tissue development. This hormonal disorder is believed to be mainly one of luteal secretions.⁶

over the whole area, usually within forty-eight hours. Promptly thereafter, recontraction of the arterioles, clotting and repair processes function, and in due time the bleeding ceases. Thus in cycle after cycle the amount and the duration of the flow are similar.

When ovulation fails, and there is no luteal hormone, estrogen from an indefinite and ever-changing number of well developed follicles establishes a bleeding potential of equally variable intensity in an endometrium that has proliferated in different degrees. According to the Smiths,⁸ "Bleeding when it does occur due to temporary drops in estrogenic support to the endometrium, fails to be accompanied by 'the trigger' mechanism of both hormonal and endometrial origin that makes for normal follicle maturation and periodicity." Furthermore, activation in the solely proliferative endometrium, unlike that in the secretory tissue, is not fairly synchronous over the whole area, often occurring in patch after patch during many days or weeks. Thus in successive periods of flow are the amount and the duration of the bleeding and the quality of the discharge variable in the absence of ovulation.

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exercises or a supporting pessary is necessary) If these measures fail, recourse may be had to the somewhat uncertain, and often not wholly satisfactory, hormones Progesterone, in doses of 10 mg on the second or third day of flow, sometimes suffices, although it may prolong the need for protection Testosterone propionate is cheaper, and in doses of 10 mg may likewise be effective An intramuscular injection of 500 units of chorion-hormone on the second day of the period is also often beneficial Unfortunately, this may cause malaise, pain in the neck and even moderate pyrexia, as if from a protein reaction Prolactin has also been favorably mentioned,¹⁴ but I have had no experience with it. I have not found extracts of ergot helpful, but others still recommend their use Nor can I endorse the use of so-called "hemostatic doses of estrogen" They seriously endanger ovulation and are almost certain to be followed by withdrawal bleeding, both of which are undesirable sequelae

In severe cases, recourse may be had to curettage, which the optimist will expect to be followed by several periods of acceptably diminished flow It is not likely to give permanent relief Since this condition is usually found in women over thirty-five, who wish, or can have, no more children, hysterectomy is not seldom the best cure

In aperiodomenorrhea, anovulation is the basic cause Ovular maturation, with consequent follicular rupture, is therefore the aim of treatment I know of no dependable or even promising method of inducing this desirable effect Nonetheless, therapeutics is not wholly futile it is easy to relieve the patient's complaints of aperiodicity and unpredictability of flow, although it is seldom possible to rectify the fundamental follicular dysfunction Time and hygiene are of appreciable assistance but should not be permitted to endow with specificity any particular method of treatment. All this can likewise be said of amenorrhea, the result of similar but more extensive ovarian deficiency With one exception, then, the treatment of both conditions is the same

Zondek¹⁵ among others discovered the secret of occasionally establishing periodicity Twenty-five milligrams of progesterone, given intramuscularly and, I believe, preferably divided into five daily doses of at least 5 mg each, can be expected to stop anovulatory bleeding and to be followed within ten days, usually within four, by satisfactory flow Rarely will more bleeding occur before twenty-eight days have passed If on the twenty-ninth day another similar series of injections is given, again flow will follow at about the same interval Properly this routine is repeated five times After six months, treatment is suspended Sometimes the extensive but immature follicular development that induced the estrogenic proliferation of the endometrium and the bleeding potential will be so repaired these processes so that flow

becomes scanty as the repetitive treatment progresses This more closely approaches the condition found in amenorrhea As in the latter disorder, some estrogen is then appropriately added to the treatment One to two milligrams of dissolved estrogen is added to each 5 mg of progesterone, or, perhaps preferably, 0.05 mg of ethinyl estradiol or about 0.3 mg of diethylstilbestrol is given orally daily during the twenty-one days preceding each series of progesterone injections

Thus is the hormonal treatment of amenorrhea and of aperiodomenorrhea essentially the same In the former, estrogen is lacking and must necessarily be added to the progesterone, since estrogen only can induce proliferation of the endometrium and establish the bleeding potential In the latter, it is not at first and may not ever be required, since the condition is inaugurated by too much estrogen and successive series of progesterone treatments may retard but may not sufficiently impede follicular growth and estrogen production

As has been said, the above treatment will, at least for a time, bring about periodic flow in both amenorrhea and aperiodomenorrhea But what is desired is ovulation that will do this and more without treatment Fortunately, in about 3 per cent of cases, especially if minimal doses of or no estrogen is needed, spontaneous ovulation ensues The Smiths^{16, 17} postulate that this may be due to a "toxin" that they have found in the endometrium as it breaks down in the process so well observed in the monkey by Markee⁵ Is this the "menotoxin" named by Schick¹⁸ in 1920 and only now approaching identification?

Other methods for inducing ovulation have received enthusiastic approval by various workers I deplore the fact that I have not found them satisfactory Small doses of x-rays have been proposed (Mazer and Israel¹⁹ and Rock, Bartlett et al²⁰) This method sometimes increases the impediment to ovulation, and may possibly have a deleterious effect on the genes of all primitive ova Gonadotropic extracts of mare's serum, as well as those from the pituitary glands of sheep, alone or preceding the injection of chorion-hormone, are apparently effective in other hands^{13, 21} The serum gonadotropins and pituitary extracts sometimes stimulate follicular growth and so evoke a modicum of bleeding in amenorrhea, but in the rare case in which ovulation has occurred, it seems to me to have been only coincidental Chorion-hormone has happily outlived its fictitious value as a follicular stimulant More potent extracts of animal anterior pituitary glands or the synthesis of the active follicle-stimulating and luteinizing hormones is hopefully awaited

A word should be said of the use of thyroid as an ovarian stimulant It is surely not a specific but may rarely help in cases with normal basal metabolic rates and more frequently in those whose rates are below normal

32 Cumberland Avenue

DISORDER IN FREQUENCY, DURATION AND AMOUNT OF FLOW

Aperiodomenorrhea

By derivation, aperiodomenorrhea means immeasurability and therefore unpredictability of the onset and of the quality, quantity and duration of flow. Under this diagnosis fall the vast majority of menstrual complaints, only amenorrhea and hypermenorrhea approaching it in frequency, although the incidence of other deviations may be greater. Reconsideration of what has been written concerning the role of the corpus luteum in regulating the maturation of ova, and the oxidation of estrogen, will disclose that in aperiodomenorrhea the basic fault is in the formation of a luteal body. Since there is no clear evidence that, in human beings ova are not matured and released without subsequent formation of a corpus luteum, and vice versa, or that this gland ever forms without preliminary rupture of the ripe follicle, it may be assumed that in this condition there is failure of ovulation. Biopsy and surgical inspection substantiate this. Follicles grow and nearly ripen in varying numbers for variable periods, but none pass the rupture stage. I say "none", but this is only a manner of speaking: the anovulatory woman may ovulate anytime. Hence, interspersed among months of ovulatory dysfunction there may occur an unrecognized normal cycle. Such cases are rare. Once a corpus luteum is formed, a succession of functional periods usually follows.

The affected patient is identified by the record of her phases of flow. Whenever in incidence they vary widely, sometimes by not much more than 28 ± 4 days, and, as is usually the case with such irregularity, they likewise vary in duration, quality and quantity of flow, this aperiodicity, this immeasurability, is sure to be associated with the presence of unruptured follicles and the absence of a corpus luteum. This is what the writers of a decade ago argued about as "anovulatory menstruation," and what before that was called "dysfunctional flow," "uterine dysfunction," "uterine insufficiency" or "metropathia haemorrhagica," and what frequently still is, I think, fuzzily dubbed "menometrorrhagia."

It is not infrequently interrupted by long or short sessions of amenorrhea, for the causal ovarian dysfunction common to both conditions varies within them only in degree of follicular development. Oligomenorrhea may resemble it, since here, too, the long cycles vary in length, but there is one clear distinction—in oligomenorrhea the phases of flow, when they come, are similar in duration, quality and quantity, whereas in aperiodomenorrhea, these vary in easily perceptible degree.

TREATMENT

The objectives of treatment for several of the disorders of menstruation are clear: the means, unfortunately, are not. As regular ovulation at intervals of about twenty-nine days, with subsequent

flow requiring an average of about three napkins a day for about five days, is considered an acceptable "curse" by most women, such is the therapist's objective. As will be seen, the methods at hand for controlling ovulation, apart from suppressing it, are lamentably deficient. When, therefore, it occurs, even but rarely, as in oligomenorrhea, nothing but general hygienic measures and encouragement should be used. The same is true for most cases of true, functional polymenorrhea, which are fortunately not frequent. We have no means for retarding ovulation without endangering it. In the occasional case of polymenorrhea, when the shortening of the cycle is due to a premature decadence of the corpus luteum, daily increments of 0.1 or 0.2 mg. of diethylstilbestrol may be tried. This has been shown in the laboratory to stimulate the gonadotropic activity of the hypophysis,¹² and in the clinic, to delay menstruation, possibly by the same process. In larger doses, and indeed occasionally in those mentioned, it may have the undesired effect of estrogen in general—that of inhibiting ovulation.

Here it is pertinent to mention those cases of infertility with apparently normal menstruation in which biopsy shows that ovulation is delayed and yet flow occurs within the normal time, because the corpus-luteum phase is comparatively curtailed and catamenia takes place from an only partially developed predecidua. Davis and Hamblen¹³ have designated these patients as those "bleeding from immature progestational endometrium." For such, treatment with small doses of diethylstilbestrol may also be helpful.

Wholesome neglect is proper in cases of noticeable ovulatory bleeding at the so-called "midperiod," a condition that is a kind of pseudopolymenorrhea. In suppressing it one may easily upset the hormonal balance on which normal ovulation depends. Patients with it are best reassured and let alone.

Because also to increase flow there is no dependable means that may not interfere with the ovulatory mechanism, no treatment but general medicine is indicated in hypomenorrhea. To be sure the emergence of this type of catamenia after years of more classic performance may occasionally presage the approaching climacteric. Even so, general supportive measures must suffice.

In hypermenorrhea, as in aperiodomenorrhea, the possibility of endometrial cancer must be ruled out by the prompt success of treatment or by curettage. Inspection of the cervix must be meticulous, and biopsy freely done.

When hypermenorrhea is of such a degree as to be very troublesome or to entail the loss with each catamenia of more blood than is easily replaced in the intervals between periods, something must be done. Attention should be directed first to the non-hormonal factors of bleeding: anemia must be relieved, the diet must be perfected, and pelvic congestion must be alleviated (often only knee-chest

exercises or a supporting pessary is necessary) If these measures fail, recourse may be had to the somewhat uncertain, and often not wholly satisfactory, hormones Progesterone, in doses of 10 mg on the second or third day of flow, sometimes suffices, although it may prolong the need for protection Testosterone propionate is cheaper, and in doses of 10 mg may likewise be effective An intramuscular injection of 500 units of chorion-hormone on the second day of the period is also often beneficial Unfortunately, this may cause malaise, pain in the neck and even moderate pyrexia, as if from a protein reaction Prolactin has also been favorably mentioned,¹⁴ but I have had no experience with it. I have not found extracts of ergot helpful, but others still recommend their use Nor can I endorse the use of so-called "hemostatic doses of estrogen" They seriously endanger ovulation and are almost certain to be followed by withdrawal bleeding, both of which are undesirable sequelae

In severe cases recourse may be had to curettage, which the optimist will expect to be followed by several periods of acceptably diminished flow It is not likely to give permanent relief Since this condition is usually found in women over thirty-five, who wish, or can have no more children, hysterectomy is not seldom the best cure

In aperiodomenorrhea, anovulation is the basic cause Ovular maturation, with consequent follicular rupture, is therefore the aim of treatment I know of no dependable or even promising method of inducing this desirable effect Nonetheless, therapeutics is not wholly futile it is easy to relieve the patient's complaints of aperiodicity and unpredictability of flow, although it is seldom possible to rectify the fundamental follicular dysfunction Time and hygiene are of appreciable assistance but should not be permitted to endow with specificity any particular method of treatment All this can likewise be said of amenorrhea, the result of similar but more extensive ovarian deficiency With one exception, then, the treatment of both conditions is the same

Zondek¹⁵ among others discovered the secret of occasionally establishing periodicity Twenty-five milligrams of progesterone, given intramuscularly and, I believe, preferably divided into five daily doses of at least 5 mg each, can be expected to stop anovulatory bleeding and to be followed within ten days, usually within four, by satisfactory flow Rarely will more bleeding occur before twenty-eight days have passed If on the twenty-ninth day another similar series of injections is given, again flow will follow at about the same interval Properly this routine is repeated five times After six months, treatment is suspended Sometimes the extensive but immature follicular development that induced the estrogenic proliferation of the endometrium and the bleeding potential will be so retard

becomes scanty as the repetitive treatment progresses This more closely approaches the condition found in amenorrhea As in the latter disorder, some estrogen is then appropriately added to the treatment One to two milligrams of dissolved estrogen is added to each 5 mg of progesterone, or, perhaps preferably, 0.05 mg of ethinyl estradiol or about 0.3 mg of diethylstilbestrol is given orally daily during the twenty-one days preceding each series of progesterone injections

Thus is the hormonal treatment of amenorrhea and of aperiodomenorrhea essentially the same In the former, estrogen is lacking and must necessarily be added to the progesterone, since estrogen only can induce proliferation of the endometrium and establish the bleeding potential In the latter, it is not at first and may not ever be required, since the condition is inaugurated by too much estrogen and successive series of progesterone treatments may retard but may not sufficiently impede follicular growth and estrogen production

As has been said the above treatment will, at least for a time, bring about periodic flow in both amenorrhea and aperiodomenorrhea But what is desired is ovulation that will do this and more without treatment Fortunately in about 3 per cent of cases, especially if minimal doses of or no estrogen is needed, spontaneous ovulation ensues The Smiths^{16, 17} postulate that this may be due to a "toxin" that they have found in the endometrium as it breaks down in the process so well observed in the monkey by Markee⁵ Is this the "menotoxin" named by Schick¹⁸ in 1920 and only now approaching identification?

Other methods for inducing ovulation have received enthusiastic approval by various workers I deplore the fact that I have not found them satisfactory Small doses of x-rays have been proposed (Mazer and Israel¹⁹ and Rock Bartlett et al²⁰) This method sometimes increases the impediment to ovulation, and may possibly have a deleterious effect on the genes of all primitive ova Gonadotropic extracts of mare's serum as well as those from the pituitary glands of sheep, alone or preceding the injection of chorion-hormone, are apparently effective in other hands^{21, 22} The serum gonadotropins and pituitary extracts sometimes stimulate follicular growth and so evoke a modicum of bleeding in amenorrhea, but in the rare case in which ovulation has occurred, it seems to me to have been only coincidental Chorion-hormone has happily outlived its fictitious value as a follicular stimulant More potent extracts of animal anterior pituitary glands or the synthesis of the active follicle-stimulating and luteinizing hormones is hopefully awaited

A word should be said of the use of thyroid as an ovarian stimulant. It is surely not a specific but may rarely help in cases with normal basal metabolic rates and more frequently in those whose rates are below normal

32 Cumberland Avenue

DISORDER IN FREQUENCY, DURATION AND AMOUNT OF FLOW

Aperiodomenorrhea

By derivation, aperiodomenorrhea means immeasurability and therefore unpredictability of the onset and of the quality, quantity and duration of flow. Under this diagnosis fall the vast majority of menstrual complaints, only amenorrhea and hypermenorrhea approaching it in frequency, although the incidence of other deviations may be greater. Reconsideration of what has been written concerning the role of the corpus luteum in regulating the maturation of ova, and the oxidation of estrogen, will disclose that in aperiodomenorrhea the basic fault is in the formation of a luteal body. Since there is no clear evidence that, in human beings ova are not matured and released without subsequent formation of a corpus luteum, and vice versa, or that this gland ever forms without preliminary rupture of the ripe follicle, it may be assumed that in this condition there is failure of ovulation. Biopsy and surgical inspection substantiate this. Follicles grow and nearly ripen in varying numbers for variable periods, but none pass the rupture stage. I say "none", but this is only a manner of speaking the anovulatory woman may ovulate anytime. Hence, interspersed among months of ovulatory dysfunction there may occur an unrecognized normal cycle. Such cases are rare. Once a corpus luteum is formed, a succession of functional periods usually follows.

The affected patient is identified by the record of her phases of flow. Whenever in incidence they vary widely, sometimes by not much more than 28 ± 4 days, and, as is usually the case with such irregularity, they likewise vary in duration, quality and quantity of flow, this aperiodicity, this immeasurability, is sure to be associated with the presence of unruptured follicles and the absence of a corpus luteum. This is what the writers of a decade ago argued about as "anovulatory menstruation," and what before that was called "dysfunctional flow," "uterine dysfunction," "uterine insufficiency" or "metropathia haemorrhagica," and what frequently still is, I think, fuzzily dubbed "menometrorrhagia."

It is not infrequently interrupted by long or short sessions of amenorrhea, for the causal ovarian dysfunction common to both conditions varies within them only in degree of follicular development. Oligomenorrhea may resemble it, since here, too, the long cycles vary in length, but there is one clear distinction — in oligomenorrhea the phases of flow, when they come, are similar in duration, quality and quantity, whereas in aperiodomenorrhea, these vary in easily perceptible degree.

TREATMENT

The objectives of treatment for several of the disorders of menstruation are clear the means, unfortunately, are not. As regular ovulation at intervals of about twenty-nine days, with subsequent

flow requiring an average of about three napkins a day for about five days, is considered an acceptable "curse" by most women, such is the therapist's objective. As will be seen, the methods at hand for controlling ovulation, apart from suppressing it, are lamentably deficient. When, therefore, it occurs, even but rarely, as in oligomenorrhea, nothing but general hygienic measures and encouragement should be used. The same is true for most cases of true, functional polymenorrhea, which are fortunately not frequent. We have no means for retarding ovulation without endangering it. In the occasional case of polymenorrhea, when the shortening of the cycle is due to a premature decadence of the corpus luteum, daily increments of 0.1 or 0.2 mg of diethylstilbestrol may be tried. This has been shown in the laboratory to stimulate the gonadotropic activity of the hypophysis,¹² and in the clinic, to delay menstruation, possibly by the same process. In larger doses, and indeed occasionally in those mentioned, it may have the undesired effect of estrogen in general — that of inhibiting ovulation.

Here it is pertinent to mention those cases of infertility with apparently normal menstruation in which biopsy shows that ovulation is delayed and yet flow occurs within the normal time, because the corpus-luteum phase is comparatively curtailed and catamenia takes place from an only partially developed predecidua. Davis and Hamblen¹³ have designated these patients as those "bleeding from immature progesterational endometrium." For such, treatment with small doses of diethylstilbestrol may also be helpful.

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the lungs. He was given morphine and 'amino-phyllin, and an oxygen mask was used. He expired on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR J SIDNEY STILLMAN. We have a man with a fifteen-year course of kidney disease who came to the hospital for the last three days of his illness, during which time certain observations were made. We can say that this man had Bright's disease, but to be more specific is not so easy. In my experience it is not only difficult clinically but sometimes pathologically to establish the exact sequence of events in the development of kidney disease.

In discussing this case it seems desirable first to attempt to determine the anatomic type of Bright's disease from which this patient died. Then, if time permits, we can take up the complications and the disturbances in body chemistry. I believe that the following diagnoses should be considered in the differential diagnosis: chronic glomerulonephritis, arteriolar nephrosclerosis, chronic pyelonephritis and polycystic disease of the kidneys.

There are no physical findings or x-ray evidence to support the last diagnosis. The presence of hypertension and the abnormal urinary findings fifteen years before death are also against it. Apparently there had been no bouts of infection and only one of gross hematuria, whereas one would expect more infection and hematuria in polycystic disease. This diagnosis must be considered, however, because it is known that patients suffering from it show evidence of renal failure between the ages of forty and fifty, and that the disease is slowly progressive. I doubt that he would have had hypertension so long before death, so I am in favor of discarding the diagnosis of polycystic disease of the kidneys.

The other three diagnoses are the likeliest possibilities. In the end stage, which was all that was observed in this hospital, they are difficult to differentiate. I am forced, however, to discard the diagnosis of chronic pyelonephritis because I can find no evidence in the history of an initiating attack of acute pyelonephritis or of recurrent attacks of headache, fever, backache and pyuria. Furthermore, the findings in the urine fifteen years before entry are not typical of this disease.

This brings us to a choice between chronic glomerulonephritis and arteriolar nephrosclerosis, and I find it a difficult one. When it was first discovered fifteen years before death, that the patient had kidney disease, the urine showed albumin, red cells and casts, and there was also a slight hypertension. If we knew which abnormality had appeared first, our problem would be easier. The fact that these urinary findings were accompanied by only a slight degree of hypertension favors chronic glomerulonephritis. The duration of the disease

from the time of discovery to death in a man of his age also points to chronic glomerulonephritis, which frequently has a long latent period. Gross hematuria, which he had on one occasion, occurs in nephrosclerosis but is more frequently found in glomerulonephritis. In comparing the degree of hypertension attained in the terminal phase in large series of cases of each disease one finds a higher average level in nephrosclerosis. In either group, however, it varies greatly in individual cases. It should also be pointed out that it is somewhat unusual for the blood pressure to rise so early in glomerulonephritis as it did in this patient. Another thing that makes me tend toward the diagnosis of glomerulonephritis is again a statistical one, namely, that only 10 per cent of patients with nephrosclerosis die from renal insufficiency; the rest dying of heart failure, vascular accidents or intercurrent infection. In this patient there was evidence of only slight to moderate cardiac hypertrophy, the left border of the heart being only 9 cm from the midline, and I believe that in nephrosclerosis of this severity one is likelier to observe greater cardiac enlargement. For these reasons I favor chronic glomerulonephritis as being the initial kidney disease from which this man suffered. With his degree of hypertension one would expect arteriolar changes to have developed in the terminal phase.

During the last eight weeks of life, the patient developed uremia, which probably accounts for the appearance of dysuria, diarrhea, vomiting, anorexia, fatigue and sleepiness. I believe that the muscular irritability was due to a low blood calcium, which is the indirect result of the inability of the kidney to eliminate phosphates. As a result of the low blood calcium the parathyroid glands are stimulated, resulting in hyperplasia of these glands and some decalcification of the bones.

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CASE 31521

PRESENTATION OF CASE

A forty-three-year-old carpenter entered the hospital complaining of vomiting.

Fifteen years before admission, during a life-insurance examination, albumin (400 mg per 100 cc), casts and a few red cells were found in the urine. At that time the blood pressure was 150 systolic, 100 diastolic. Five years before admission he noted the onset of nocturia, which became progressively worse. At about the same time he had episodes of epigastric pain after meals, which were relieved by food and soda. A duodenal ulcer was diagnosed and treated with Sippy powders and frequent feedings. The symptoms subsided, but the patient continued to have occasional attacks of epigastric discomfort. Ten months before admission he had an episode of pain in the right flank and costovertebral angle, followed by hematuria of one week's duration. Some time later he noted the onset of cramps in the legs and abdomen, restlessness and twitching of the eyelids. Eight weeks before admission he began to vomit, losing a large part of all food ingested. The vomitus occasionally resembled coffee grounds. Progressive dryness and scaliness of the skin appeared, with itching

He also complained of dyspnea, fatigue, anorexia, diarrhea (one to five watery stools daily), polydipsia and sleepiness during the day. Diminution of auditory and visual acuity, with photophobia, occurred. Frequency, nocturia and dysuria became worse. During this period he had lost 10 pounds.

On physical examination, the patient was pale and thin. The skin was dry, scaling and cold. The breath had a uremic odor. The eyelids were red-den, with fissuring of the lid margins. The pupils reacted to light and accommodation. Examination of the eyegrounds showed arterial narrowing and arteriovenous nicking. A "wooly" exudate and flame-shaped hemorrhages were present. The lips were cracked, and the oral mucous membranes pale. The left border of the heart was 9 cm to the left of the midline in the fifth interspace. The cardiac rhythm was regular. The lungs were clear. The abdomen was slightly tense and tympanic. The ankles showed pitting edema. Neurologic examination was negative.

The temperature was 97.4°F, the pulse 78, and the respirations were 24. The blood pressure was 185 systolic, 110 diastolic.

The red-cell count was 1,580,000, with 4.9 gm of hemoglobin. The white-cell count was 9800, with 70 per cent neutrophils. The red cells showed marked anisocytosis and poikilocytosis and moderate achromia. The urine was yellow, cloudy and acid, with a specific gravity of 1.010. It gave a +++ test for albumin, there was no sugar, but the sediment contained many granular casts, 5 to 10 white cells and 100 red cells per high-power field. Many clumps of epithelial cells and white cells were present. The nonprotein nitrogen was 230 mg per 100 cc, total protein 6.7 gm per 100 cc, the sodium 144 milliequiv per liter, and the chloride 95 milliequiv.

The patient became markedly dyspneic and orthopneic. Numerous bubbling rales were heard in

*On leave of absence

the lungs. He was given morphine and 'amino-phyllin, and an oxygen mask was used. He expired on the third hospital day.

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On physical examination, the patient was pale and thin. The skin was dry, scaling and cold. The breath had a uremic odor. The eyelids were reddened, with fissuring of the lid margins. The pupils reacted to light and accommodation. Examination of the eyegrounds showed arterial narrowing and arteriovenous nicking. A "wooly" exudate and flame-shaped hemorrhages were present. The lips were cracked, and the oral mucous membranes pale. The left border of the heart was 9 cm to the left of the midline in the fifth interspace. The cardiac rhythm was regular. The lungs were clear. The abdomen was slightly tense and tympanitic. The ankles showed pitting edema. Neurologic examination was negative.

The temperature was 97.4°F, the pulse 78, and the respirations were 24. The blood pressure was 185 systolic, 110 diastolic.

The red-cell count was 1,580,000, with 4.9 gm of hemoglobin. The white-cell count was 9800, with 70 per cent neutrophils. The red cells showed marked anisocytosis and poikilocytosis and moderate achromia. The urine was yellow, cloudy and acid, with a specific gravity of 1.010. It gave a +++ test for albumin, there was no sugar, but the sediment contained many granular casts, 5 to 10 white cells and 100 red cells per high-power field. Many clumps of epithelial cells and white cells were present. The nonprotein nitrogen was 230 mg per 100 cc, total protein 6.7 gm per 100 cc, the sodium 144 milliequiv per liter, and the chloride 95 milliequiv.

The patient became markedly dyspneic and orthopneic. Numerous bubbling rales were heard in

*On leave of absence

the lungs. He was given morphine and aminophyllin, and an oxygen mask was used. He expired on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR J SIDNEY STILLMAN. We have a man with a fifteen-year course of kidney disease who came to the hospital for the last three days of his illness, during which time certain observations were made. We can say that this man had Bright's disease, but to be more specific is not so easy. In my experience it is not only difficult clinically but sometimes pathologically to establish the exact sequence of events in the development of kidney disease.

In discussing this case it seems desirable first to attempt to determine the anatomic type of Bright's disease from which this patient died. Then, if time permits, we can take up the complications and the disturbances in body chemistry. I believe that the following diagnoses should be considered in the differential diagnosis: chronic glomerulonephritis, arteriolar nephrosclerosis, chronic pyelonephritis and polycystic disease of the kidneys.

There are no physical findings or x-ray evidence to support the last diagnosis. The presence of hypertension and the abnormal urinary findings fifteen years before death are also against it. Apparently there had been no bouts of infection and only one of gross hematuria, whereas one would expect more infection and hematuria in polycystic disease. This diagnosis must be considered, however, because it is known that patients suffering from it show evidence of renal failure between the ages of forty and fifty, and that the disease is slowly progressive. I doubt that he would have had hypertension so long before death, so I am in favor of discarding the diagnosis of polycystic disease of the kidneys.

The other three diagnoses are the likeliest possibilities. In the end stage, which was all that was observed in this hospital, they are difficult to differentiate. I am forced, however, to discard the diagnosis of chronic pyelonephritis because I can find no evidence in the history of an initiating attack of acute pyelonephritis or of recurrent attacks of headache, fever, backache and pyuria. Furthermore, the findings in the urine fifteen years before entry are not typical of this disease.

This brings us to a choice between chronic glomerulonephritis and arteriolar nephrosclerosis, and I find it a difficult one. When it was first discovered fifteen years before death, that the patient had kidney disease, the urine showed albumin, red cells and casts, and there was also a slight hypertension. If we knew which abnormality had appeared first, our problem would be easier. The fact that these urinary findings were accompanied by only a slight degree of hypertension favors chronic glomerulonephritis. The duration of the disease

from the time of discovery to death in a man of his age also points to chronic glomerulonephritis, which frequently has a long latent period. Gross hematuria, which he had on one occasion, occurs in nephrosclerosis but is more frequently found in glomerulonephritis. In comparing the degree of hypertension attained in the terminal phase in large series of cases of each disease one finds a higher average level in nephrosclerosis. In either group, however, it varies greatly in individual cases. It should also be pointed out that it is somewhat unusual for the blood pressure to rise so early in glomerulonephritis as it did in this patient. Another thing that makes me tend toward the diagnosis of glomerulonephritis is again a statistical one, namely, that only 10 per cent of patients with nephrosclerosis die from renal insufficiency; the rest dying of heart failure, vascular accidents or intercurrent infection. In this patient there was evidence of only slight to moderate cardiac hypertrophy, the left border of the heart being only 9 cm from the midline, and I believe that in nephrosclerosis of this severity one is likelier to observe greater cardiac enlargement. For these reasons I favor chronic glomerulonephritis as being the initial kidney disease from which this man suffered. With his degree of hypertension one would expect arteriolar changes to have developed in the terminal phase.

During the last eight weeks of life, the patient developed uremia, which probably accounts for the appearance of dysuria, diarrhea, vomiting, anorexia, fatigue and sleepiness. I believe that the muscular irritability was due to a low blood calcium, which is the indirect result of the inability of the kidney to eliminate phosphates. As a result of the low blood calcium the parathyroid glands are stimulated, resulting in hyperplasia of these glands and some decalcification of the bones.

I have disregarded the history of ulcer, which might have accounted for the vomiting and in turn for the high level of the blood nonprotein nitrogen and also a value for the total protein that is higher than what I should have expected in a patient with this amount of kidney disease.

In conclusion, then, I favor the diagnoses of chronic glomerulonephritis, with renal insufficiency and uremia, hypertensive heart disease, with slight to moderate cardiac hypertrophy, and questionable hyperplasia of the parathyroid glands with accompanying osteitis fibrosa.

DR CHESTER M JONES. This man represents one of the cases that never should have had alkaline therapy. If he had had it for a year continuously, the renal situation might have been aggravated, and that, accompanied by a milk diet, might have produced renal calculi.

CLINICAL DIAGNOSES

Chronic glomerulonephritis
Pulmonary edema

DR STILLMAN'S DIAGNOSES

Chronic glomerulonephritis
Hypertensive heart disease
Parathyroid hyperplasia, secondary?

ANATOMICAL DIAGNOSES

Subacute and chronic glomerulonephritis developing in congenital polycystic kidneys

Bronchopneumonia
Parathyroid hyperplasia, secondary
Duodenal ulcer, healed

PATHOLOGICAL DISCUSSION

DR RONALD C SNIFFEN As expected, the primary disease was found in the kidneys. The left was enlarged to 200 gm, whereas the right was slightly below the average normal weight of 150 gm. Their surfaces were granular and somewhat pale, and the entire parenchyma, both medulla and cortex, contained thin-walled cysts, which varied in size from that of a pinhead to over 10 cm in diameter and were filled with yellowish watery fluid (Fig 1). In

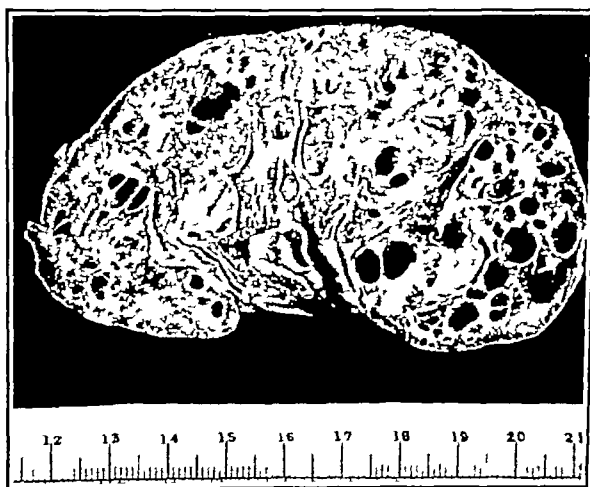


FIGURE 1 Photograph of Left Kidney

brief, they were typical polycystic kidneys, but there seemed to be an unusual amount of unaffected parenchyma for this man to have died in uremia. Sections showed microscopically the usual picture of polycystic kidneys. The remaining parenchyma, however, revealed the unmistakable changes of subacute and chronic glomerulonephritis (Fig 2). There was pronounced vascular damage, and some of the glomerular tufts were acutely inflamed.

In addition there was a bronchopneumonia as well as evidence of a healed duodenal ulcer. The parathyroid glands were slightly hyperplastic, but bone changes had not yet appeared. The heart was only slightly, if at all, hypertrophied, weighing 370 gm.

CASE 31522

PRESENTATION OF CASE

A sixty-two-year-old man was admitted to the Emergency Ward complaining of abdominal pain.

Five days before admission he noticed cramping, generalized abdominal pain, which persisted and became somewhat severer. He lost his appetite and became nauseated, but there was no vomiting, jaundice or melena. There had been no recent weight loss.

Eight months before admission he had had an episode of cramping pain low in the abdomen, which subsided in five days. Two years before admission bright-red blood was seen in the stools on

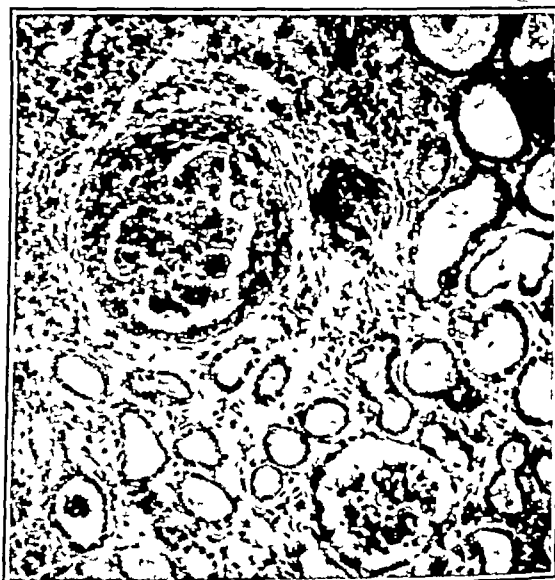


FIGURE 2 Photomicrograph of a Section of the Left Kidney. Note the glomerular changes characteristic of glomerulonephritis.

one occasion, following this, constipation developed and increased. The stools had never been tarry. Bitter gaseous eructations were noted, with occasional vomiting. There had been no hematuria.

Physical examination revealed a systolic murmur heard at the base of the heart. The lungs were normal. The abdomen was moderately distended, with generalized tenderness, particularly over a mass to the right of the umbilicus. This mass measured about 10 by 5 cm, and was dull to percussion; the mass was not fixed but did not move on respiration. It did not seem to be connected with the kidney or liver. Peristalsis was active. Rectal examination was negative.

The temperature was 102°F, the pulse 110, and the respirations 30.

Examination of the blood revealed a white-cell count of 25,200. The urine was normal. Stomach contents and a stool were guaiac negative.

After two days in the Emergency Ward, the white-cell count rose to 33,100 and the patient was admitted to the hospital. The abdominal pain was

subsiding. He had had two watery brown stools a day. The temperature was 99°F, and the blood pressure 120 systolic, 74 diastolic. The heart was not enlarged. A systolic murmur was heard over the base of the heart, transmitted to the apex and axilla. The pulse was strong and regular, at a rate of 88. The left shoulder was low, and expansion of the left chest was markedly decreased. The left half of the diaphragm was 2 to 3 cm higher than the right half. An expiratory friction rub was heard all over the left chest, most marked at the base. There were a few fine rales in both bases. The abdominal mass was still present but less tender than before. Abdominal distention persisted, with normal peristalsis. There was no costovertebral angle tenderness.

During his stay in the hospital the white-cell count decreased steadily. The red-cell count was 4,500,000. On the third hospital day the nonprotein nitrogen was 32 mg per 100 cc, the total protein 5.6 gm, and the chloride 94 milliequiv per liter. The serum amylase was 39 units per 100 cc (normal 15 to 35 units).

A flat film of the abdomen showed the colon to be filled with gas and fecal material over to the splenic flexure. Distal to this the bowel was outlined with gas without evidence of retained fecal material. No soft-tissue mass was recognized. The bones and joints of the lumbar spine and pelvis were not remarkable. A barium enema filled a loop of sigmoid that rose high out of the pelvis into the left upper quadrant. There was no rigidity of the wall. The remainder of the colon filled without evidence of disease. The mucosal pattern after evacuation was not remarkable. The appendix filled, but the terminal ileum did not. A small area of calcification lay to the right of the first lumbar interspace 4.5 cm from the spine. A gastrointestinal series was negative. An intravenous pyelogram revealed normal kidney outlines. The psoas muscles were symmetrical. The liver and spleen were not enlarged. The intravenous dye was excreted promptly and in good concentration, outlining non-dilated upper urinary passages. The bladder shadow was not remarkable. There was another indefinite area of calcification medial to that previously described. It could not be localized. On a chest plate, the lung fields were clear, as were the costophrenic sinuses. The diaphragm was limited in motion. The heart was within normal limits. The aorta was markedly tortuous. A Graham test showed a gall bladder filled with well concentrated dye. Following a fatty meal the gall bladder was seen to contract.

An operation was performed on the seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. OLIVER B. COPE. I should like to ask when the serum amylase test was done.

DR. BENJAMIN CASTLEMAN. It was done four days after admission.

DR. COPE. The amylase test used in this hospital is based on the amount of reducing sugar produced from starch after fifteen minutes of incubation of the patient's blood serum with starch. The normal values range between 15 and 35 units. This reading of 39 is therefore just above the limit of normal.

After reading this record I can entertain but one diagnosis and that is acute pancreatitis. Let me tell you why I make that diagnosis. The history is not too characteristic or too helpful. It fits with many conditions, but I take some comfort from the apparent difficulty that the service had in making a diagnosis in the first days.

On physical examination there were a tender abdominal mass and intestinal distention. There was initially nothing to indicate that this mass was retroperitoneal beyond the fact that it did not move with respiration. One could properly consider several retroperitoneal masses, such as aortic aneurysm, for instance, but these I shall pass over. The mass might have been an acutely inflamed, low-lying gall bladder, not intimately bound to the liver. In two days, however, there were signs that the left side of the diaphragm was elevated, and the mass is recorded as less tender. It would be hard to tie together decreasing inflammation of a right-sided gall bladder and the simultaneous development of a high diaphragm on the left. But such a dual involvement of right and left sides is characteristic of acute pancreatitis, for with the spread of inflammation out from the body and tail of the pancreas into the lesser peritoneal cavity, elevation and fixation of the left half of the diaphragm is the rule, even though no mass may be felt on the left side of the abdomen. The right subdiaphragmatic space is not similarly involved because the liver blocks the way. That the mass and origin of the elevation of the left diaphragm did not lie in the urinary tract is suggested by the absence of costovertebral tenderness and the unlikelihood of spread of inflammation from the right kidney to the left subdiaphragmatic space.

That acute pancreatitis became apparent as a possible diagnosis is indicated since on the fourth hospital day a serum amylase test was made. The x-ray examination offers comforting confirmation of this point of view. The right kidney and the intestinal tract are excluded as sources of the mass. There is partial obstruction of the colon at the splenic flexure, and at first sight there would seem to be disease of the colon. One cannot, however, put together obstruction of the splenic flexure, a right-sided mass and primary disease of the colon. But this triad is just what acute inflammatory disease of the pancreas can do. A considerable mass can be produced by inflammation in the pancreas and retroperitoneal area, and it can, and indeed occasionally does, simulate large-bowel intestinal

obstruction Not long ago we had a patient with obstruction at the hepatic flexure with a positive diagnosis by x-ray of carcinoma of the hepatic flexure that turned out to be pancreatitis A mass arising in the head of the pancreas on the right side had projected laterally, compressing the right colon The findings in the colon here could be explained by a massive pancreas, the body and tail of the pancreas involving the splenic flexure It could also account for the high diaphragm on the left, because there may be a considerable amount of fluid in the lesser peritoneal cavity Indeed, there may be diaphragmatic pleurisy and fluid in the chest I suspect that the surgeon went in to drain a large accumulation of fluid These accumulations can rapidly occur

A patient with acute pancreatitis can have a normal Graham test, but it is not usual The incidence of pancreatitis is much higher in the presence of gall-bladder disease The acute, hemorrhagic, fulminating type of pancreatitis is the one that exists more frequently in the absence of gall-bladder disease In this patient we are dealing with something much less fulminating The patient survived five days before entry and seven days in the hospital before operation, which he presumably survived It is therefore a less fulminating type of disease and is likelier to have been associated with gallstones Furthermore, a negative Graham test does not exclude small gallstones

An abdominal tap would have furnished valuable information In cases suspected of having acute pancreatitis a tap should be carried out in the left gutter of the peritoneal cavity If consommé-like fluid is withdrawn the diagnosis is virtually established, because with enzymic irritation and fat necrosis involving the peritoneal surface there is usually, in fact one might say always, an excessive amount of fluid, which has a characteristic gross appearance Not only is the color like that of consommé but there may be fat deposits floating on the surface I should like to emphasize the clinical usefulness of this single test It can be carried out safely in the early hours of the disease before there is danger of adhesion of the intestinal wall to the parietal peritoneum The serum amylase test in acute pancreatitis is also diagnostic In this case it was done nine days after the onset of the disease, and although it is a borderline value, it does not exclude the diagnosis in this patient The characteristic curve of the amylase test in both the blood serum and the urine is that it rapidly reaches a peak after the onset of the disease and slowly subsides, it may be normal at the end of seven days, so that one cannot be absolute about the diagnosis thereafter Acute pancreatitis certainly seems to be the most logical diagnosis, and although I suspect that Dr Castleman has some trick up his sleeve to catch me, I cannot make any other diagnosis

DR FRANCIS D MOORE I should like to point out that an elevated amylase is not diagnostic It can be produced by a host of other conditions in the abdomen If it is elevated above a certain level, yes, but when it is borderline like this, I do not believe that it should be considered diagnostic

DR COPE I agree There is only one disease that I know of that gives a really high serum amylase level, namely, obstructive occlusion of the pancreatic duct and its consequences Acute pancreatitis apparently gives a comparable picture The amylase activity rises with the same sequence if the pancreatic duct is ligated at operation — a high abrupt rise, with gradual fall and return to normal Such a rise occurs following ligation of any portion of the duct, as for example following extirpation of the duodenum The explanation suggested by Elman* of St Louis is, I believe, the correct one This amylase, an enzyme, is intended for the intestinal tract It is the external secretion of the pancreas When backed up by ductal ligation associated with inflammation in the pancreatic tissue, the enzyme is absorbed into the blood stream As the inflammation subsides there is no further excess It is believed not to be the amylase enzyme that normally exists in the blood stream

CLINICAL DIAGNOSIS

Acute pancreatitis

DR COPE'S DIAGNOSIS

Acute pancreatitis

ANATOMICAL DIAGNOSIS

Acute pancreatitis, with fat necrosis

PATHOLOGICAL DISCUSSION

DR RODOLFO E HERRERA The operation was a peritoneoscopy We saw a mass to the right of the umbilicus This mass was behind the omentum and gave the impression of being retroperitoneal The entire peritoneum, anterior gastric wall, small bowel and liver were covered with small pale, yellowish implants averaging 2 mm in diameter Never having seen fat necrosis through a peritoneoscope I did not know whether they were fat necroses or carcinomatous implants Nor had Dr Benedict seen fat necrosis through the peritoneoscope, so we did not know which of the two it was At the time of peritoneoscopy no free fluid could be seen in the abdominal cavity, that does not mean that there was none previously We removed one of these small implants

DR CASTLEMAN The biopsy did show fat necrosis, so that there is no doubt that the disease process was acute pancreatitis The patient went home two weeks after peritoneoscopy Have you seen him since?

*Elman R. Variations of blood amylase during acute transient disease of pancreas *Ann Surg* 105 379 384 1937

DR HERRERA No By the time he went home the mass had decreased markedly in size. The abdomen was no longer tender and the temperature was within normal limits.

* * *

Addendum The patient was seen in the Out Patient Department three weeks after discharge. He was asymptomatic, and abdominal examination was negative. No mass could be felt. He returned to the Emergency Ward, however, three weeks later, just two months after the peritoneoscopy, with the story that three days before he was seized with a sudden severe pain in the right upper quadrant that radiated across the epigastrium to the

left upper quadrant. This pain was associated with nausea and vomiting. He was readmitted to the hospital.

Physical examination showed tenderness in the right upper quadrant. The serum amylase was only 11 units per 100 cc. After a Graham meal the gall bladder was not visualized, and it was decided to remove the gall bladder and to explore the common duct. At operation, fat necroses, some of them already calcified, were scattered over the pancreas and omentum. There was no evidence of an acute process. The gall bladder was removed. No stones were found in either the gall bladder or the common duct. The patient left the hospital two weeks later and was free from symptoms.

An index of the diagnoses and discussers of the Case Records for the year 1945 will be found elsewhere in this issue of the *Journal*.

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MCMXLVI

THE value of a New Year is that it brings with it, or seems to bring with it, an opportunity to wipe the slate clean of the mistakes of the dying year, and to make a fresh start. Of course we can make a fresh start at any season of the calendar, but it seems more fitting to do so at its close. New Year's Eve means curtains, and the next day starts a new act and, we always hope, a happier one.

It is a good thing to have this symbolic "fresh start" as a sign of a certain flexibility of mind — an earnest of our desire to be better and to do better in life than the frailty of our mortal cosmos had hitherto permitted. It means that, weak as we are,

we want to be good — at least those of us who make our New Year's resolutions with any degree of seriousness.

We must frequently give way to the sad reflection that not many of our happy new years of the past have remained happy for long, owing both to our own failings and to the folly of others. Life, which may be gracious, effective and productive, is filled with inner tensions and with anxieties over the curse of mankind — the drive for getting and spending or getting and keeping. The curse of acquisitiveness, of getting the better of someone else and of having more than our neighbor has, whether as an individual or as a nation, has blighted much of the happiness that might otherwise have existed in the world.

Wordsworth, in an earlier period of world unrest, felt much the same emotion when he wrote his sonnet to the world:

*The world is too much with us, late and soon,
Getting and spending, we lay waste our powers
Little we see in Nature that is ours,
We have given our hearts away, a sordid boon!*

It is not intended to imply that there is not and cannot be happiness in life, despite the destructive influences of unfavorable environmental factors. Any life can be happy if it will give to material values only their due and retain sufficient intellectual and emotional flexibility to face what the year will bring.

With this comforting thought and a firm belief in the desirability of new and better resolutions, we again find courage to wish our readers, sincerely, a Happy New Year!

ABUSE OF PENICILLIN

LAST May when the War Production Board removed the restrictions on the distribution of penicillin, there was every reason to anticipate that its use would become widespread. When the manufacturers found it possible to reduce the price to a reasonable figure, the temptation to use it even more extensively and in larger amounts became greater. In the case of the sulfonamide drugs, at least some physicians exercised reasonable caution in prescribing them because of the toxic effects that so frequently accompanied their use. The rela-

tive freedom of penicillin from toxic side effects does not impose this limitation.

It is probably fair to say that penicillin is now being used in large amounts and in many conditions irrespective of any demonstrated beneficial effects. Until recently the only reasonable restraint that many physicians felt was caused by the necessity of giving the penicillin by injection. Thus, penicillin had to be administered either by a doctor or by a trained nurse and its use was essentially limited to

hospitals or to homes in which private nursing service was available. In recent months, shortage of nurses and of hospital beds has considerably limited the ability of many physicians to prescribe the agent. Furthermore, the objections of patients themselves to repeated and prolonged injections have often reminded the physician that continuation of treatment could only

be justified by reasonable indications.

It is in the hospitals, especially the larger ones, that penicillin has been most flagrantly abused, particularly from the point of view of the quantities dispensed. Orders for penicillin have been written lavishly for all patients with fever and for most of those in whom fever or infection might be anticipated, irrespective of any possible benefits that could reasonably be expected from its use. Interns and visiting physicians alike have shared in this spree. In one large Boston hospital alone, the amount of penicillin used in the past six months was equal to the entire world production only two years ago. The amount used in a single day in October was considered quite adequate, during the period when penicillin was being rationed, to fulfill reasonably the entire needs of all the patients of the same hospital over a period of three months. In another large Boston hospital, one of its administrators made a brief survey of the use of penicillin when the amount of money expended for

this drug was found to be equal to the total amount being spent for all other drugs. It was obvious that totally excessive amounts were being given, that patients were receiving injections without any reasonable indication and that the drug was being continued almost indefinitely after the time when further benefit could be reasonably expected. Following this survey and certain recommendations, the amount used in the hospital declined from 60 to 80 per cent without interfering with the proper treatment of any patient.

It is not unlikely that the patients in the latter hospital actually benefited through this reduction in the amount of penicillin dispensed. Nursing services had been much curtailed, and the amount of nursing time that was released from unnecessary penicillin injections was undoubtedly well used for the essential care of patients. Furthermore, when penicillin

MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to

George L. Schadt, *Chairman*
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8 Fenway
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lin is not given until there is reasonable evidence that it is indicated, or if it is discontinued promptly after a brief but adequate period has demonstrated that it is not producing a desirable result the patient will benefit because then the physician will make a greater effort to arrive at a proper diagnosis and a more reasonable method of therapy.

At present, when the incidence of infections requiring penicillin therapy is greatest there is an acute shortage of penicillin. This is due to many factors not easily controlled. It would be well for physicians to take stock of their use of penicillin from time to time and to be sure that they are prescribing it in a reasonable manner. The fact that large doses may be safely given does not mean that all patients should receive these amounts which should be reserved for conditions in which big doses are clearly indicated. Furthermore, in cases in which prolonged treatment is not necessary the drug should be discontinued at the earliest possible

moment The widespread prophylactic use of penicillin in the treatment of colds or of uninfected wounds should be discouraged — particularly during the present shortage

MASSACHUSETTS MEDICAL SOCIETY

DEATH

LAWLER — William P Lawler, M D, of Lowell, died December 8 He was in his eighty-sixth year

Dr Lawler received his degree from the College of Physicians and Surgeons, Baltimore, in 1886 He was appointed to the staff of St John's Hospital in 1891, served as city physician for three years and was a member of the Lowell Board of Health from 1891 to 1894 and again from 1932 to 1935 He was appointed to represent Lowell at the Pan-American Medical Congress in 1893 He was dean of physicians in Lowell, having been a practitioner since 1888 He was president of the Middlesex North District Medical Society in 1917 Dr Lawler had been in semiretirement for several years

His widow, three daughters a son and a sister survive

MISCELLANY

DEACONESS HOSPITAL TO CELEBRATE FIFTIETH ANNIVERSARY

In commemoration of the fiftieth anniversary of New England Deaconess Hospital, a dinner will be held on Wednesday evening, January 30 at the Parker House, according to a recent announcement by Dr Warren F Cook, Administrator

Speakers will include Dr Elliott P Joslin, medical administrator of the George F Baker Diabetic Clinic, Dr Frank H Lahey, surgeon-in-chief of the hospital, Mr Everett Jones, vice-president of *Hospital Management*, Dr Nathaniel P Faxon, president of the Boston Hospital Council and director of the Massachusetts General Hospital, and Mr Howard Brewer, president of the Board of Trustees of the hospital, who will preside Head-table guests will include Dr Carl S Ell, vice-president of the Board of Trustees of the hospital, Stanley MacMullen, chairman of the Executive Committee, Mr and Mrs Ernest Howes, Mrs Alexander Grant, Mr and Mrs William Snow, Jr, Dr Charles Wilinsky, director of the Beth Israel Hospital, and other prominent civic leaders of Boston

A financial drive is now in process at New England Deaconess Hospital to obtain funds for the addition of 200 beds, which will enable the hospital to serve more than 10,000 patients annually

DIRECTORY OF APPROVED SURGICAL TRAINING PLANS

Chiefly as an aid to medical officers returning from war duty, the American College of Surgeons has published a 424-page directory in which are listed and described the approved programs of graduate training in surgery in two hundred and forty civilian hospitals in the United States and Canada, and in thirty-two Navy, seven Veterans Administration and ten United States Public Health Service hospitals The total number of approved training plans comprise two hundred and twenty-eight in general surgery and five hundred and twenty-two in the surgical specialties — fractures, plastic surgery, proctology, thoracic surgery, neurologic surgery, orthopedic surgery, urology, obstetrics and gynecology (combined and separately) and ophthalmology and otolaryngology (combined and separately) In these seven hundred and fifty training plans, approximately two thousand surgeons may be trained, whereas, as the College points out, training facilities for at least five thousand are urgently needed for returning medical veterans whose training in surgery was interrupted by their military service

Publication of the directory is expected to stimulate the formation of additional programs of training in suitable hospitals

The descriptions of the approved programs include information about the size and type of hospital, organization of the medical staff, facilities for study of the basic medical sciences in their application to surgery, library facilities, clinical material, manner of selecting individuals for training in surgery, scope and method of surgical training, supervision by the medical staff, examination and thesis requirements and provision, if any, for conferring higher medical degrees

NOTICES

Dr Leo Alexander, having returned from military service in the United States Army, announces the opening of office at 433 Marlborough Street, Boston, for the practice neurology and psychiatry

Dr Edward Blank announces the removal of his office for the practice of psychiatry and neurology from 205 E Building to 1102 West Culver, Phoenix, Arizona

Dr Jacob Brem, returning from military service, announces the reopening of his office at 796 Pleasant Street, Worcester for practice limited to the care of children

Dr Allan L Davis, having returned from military service is resuming the practice of surgery at 520 Commonwealth Avenue, Boston

Dr Rose C Munro announces that, by error, her name was omitted from the new *Telephone Directory* Her office address is Hotel Braemore, 466 Commonwealth Avenue Boston (KEN 4600) and her residence address, 128 Marlborough Street, Boston (COM 0193)

Dr Joseph A Sapienza, having returned from military service, announces the opening of his office at 12 East Haven Street, Lawrence, for the general practice of medicine and surgery

Dr Herbert Sherwin, having returned from military service has resumed the practice of pediatrics at 371 Commonwealth Avenue, Boston

Dr Claude E Welch, having returned from military service is resuming the practice of surgery at 266 Beacon Street Boston

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, January 3, at 7 15 p m in the classroom of the Nurses' Residence Dr Gull Lindh Muller will speak on the subject "Clinical Significance and Diagnosis of Jaundice"

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday January 8, at 8 15 p m There will be a symposium on deep vein thrombosis and pulmonary embolism Dr John Homan will preside

PROGRAM

Leg Venograms during Operations Dr David Davis
Femoral-Vein Ligations Dr Jacob Fine
Preliminary Report The treatment of a controlled group of patients with dicumarol Dr Gordon Donaldson
Vena-Cava and Femoral-Vein Interruptions Dr Robert R Linton
Immediate and Late Results of Deep-Vein Thrombosis Dr John B Sears

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